PIPES AND PIPEWORK

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MANUFACTURING PERFUMER

A PUBLICATION OF THE LEONARD HILL TECHNICAL GROUP

Vol. XXXII No. 10

OCTOBER 1961

top

products in Poly-Tainer plastic bottles by

METAL BOX

PLASTICS GROUP

PLASTIC FILMS · LAMINATIONS · BOTTLES · MOULDED CONTAINERS

MB55-1

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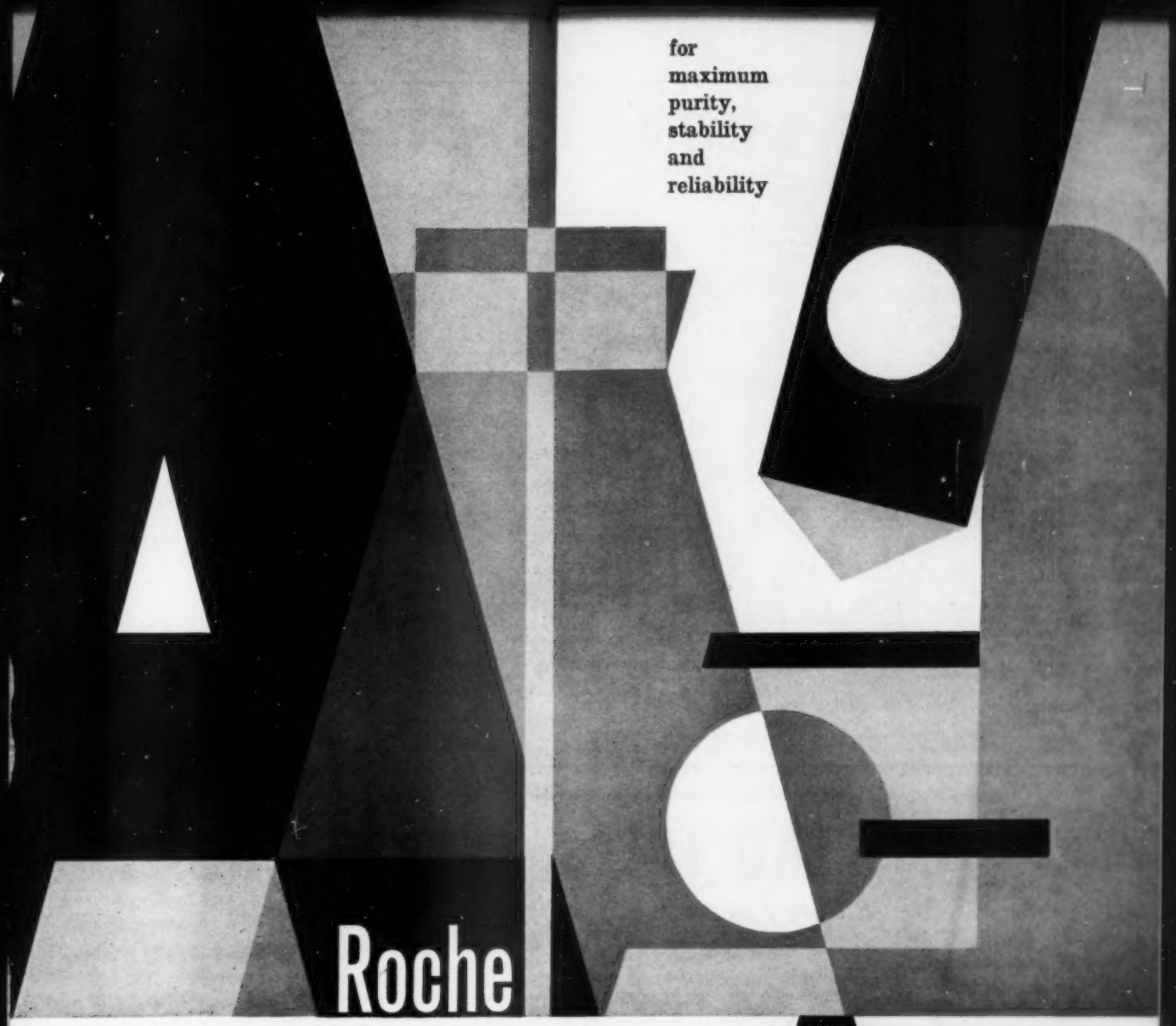

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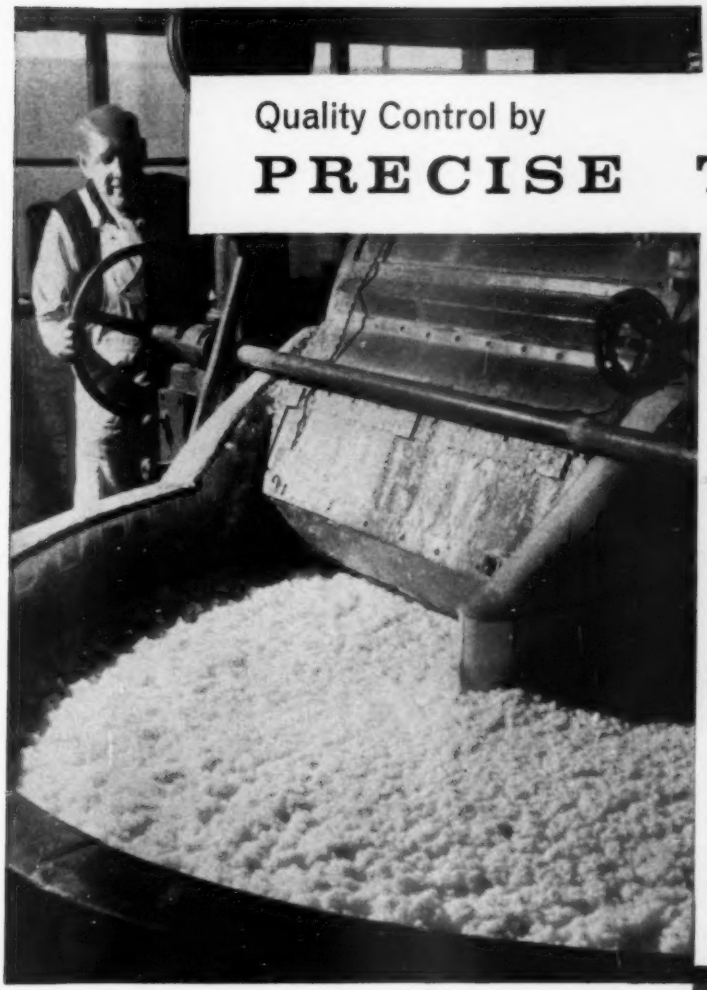

Filtration is now recognised as one of the important single operations undertaken in many manufacturing processes. Sera, blood plasma, antibiotics, pharmaceutical products, as well as beverages, are all filtered and sterilised through Ford's STERIMATS. At Ford's, research and development of filtration methods with modern equipment has resulted in technical knowledge which is second to none in this field. From their long and detailed study of the fundamental principles of filtration, Ford's have developed a series of quality control tests to ensure consistency of performance of their products. The efficiency of STERIMATS is achieved by the careful, precise admixture of asbestos fibres and cellulose, providing a mat that retains a high degree of porosity and permits a high rate of flow. STERIMATS not only filter but adsorb micro-organisms that would spoil an otherwise stable, immaculate, crystal-clear filtrate.

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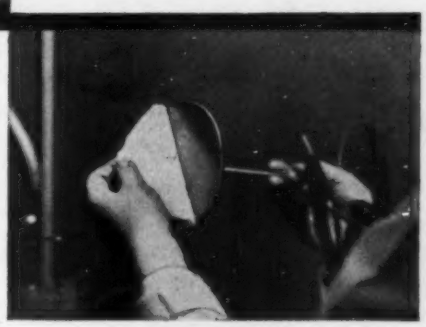
Testing wet stock. This test determines the permeability of the stock.



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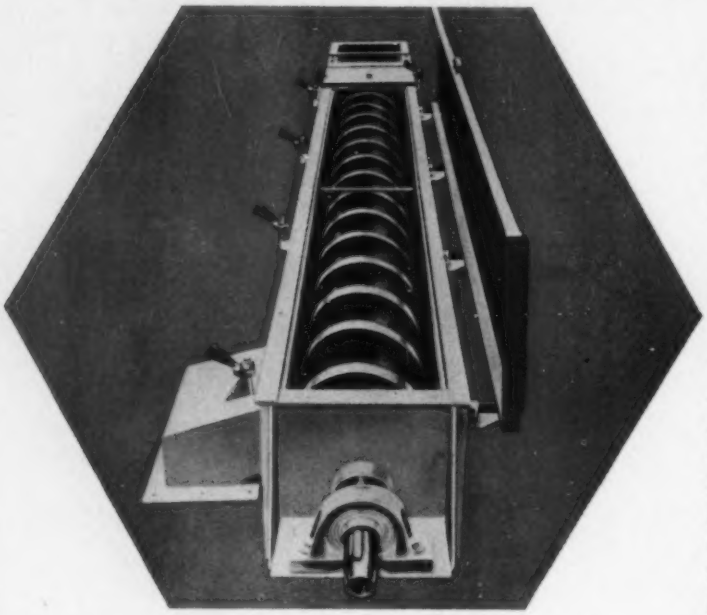
Scott-Rietz

Thermascrews for Chemical Processing



Designed for precise heating or cooling of chemicals or foodstuffs, the Scott-Rietz Thermascrew consists of a hollow conveyor screw rotating in a jacketed trough. The heating or cooling medium is circulated through both the jacket and hollow screw thus heating or cooling the material being simultaneously conveyed.

MATERIALS OF CONSTRUCTION

Scott-Rietz Thermascrews can be supplied either in mild steel, plated or stainless steel.

USES

All types are suitable for multi-pass operations, and can be adapted for evaporation, drying, crystallising, cooking, etc. on a continuous basis. For batch operations a twin screw arrangement is usually employed and the equipment can be used as a dryer, cooker, reactor, etc.
Screw diameters range from 8″ to 30″, and lengths from 8′ to 30′.

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SPECIMEN THERMASCREW SIZES

MODEL	Type	Screw Diam.	Effective Length	Approx. Heating Surface	Normal H.P.
TJ8 x 12	CONTINUOUS	8″	12′	40 sq. ft.	1
TJ12 x 10	,,	12″	10′	50 ,, ,,	1
TJ12 x 20	,,	12″	20′	100 ,, ,,	2
TJ16 x 20	,,	16″	20′	140 ,, ,,	2
TJ24 x 20	,,	24″	20′	250 ,, ,,	5
TKM12 x 12	BATCH	12″	12′	120 ,, ,,	5
TJM16 x 12	,,	16″	12′	155 ,, ,,	10

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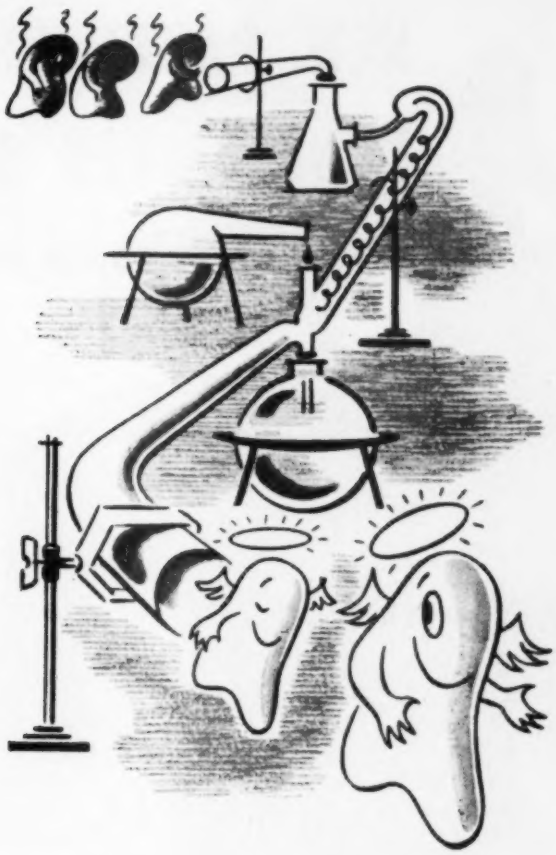

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WITH HAND OR POWER OPERATED DISCHARGE

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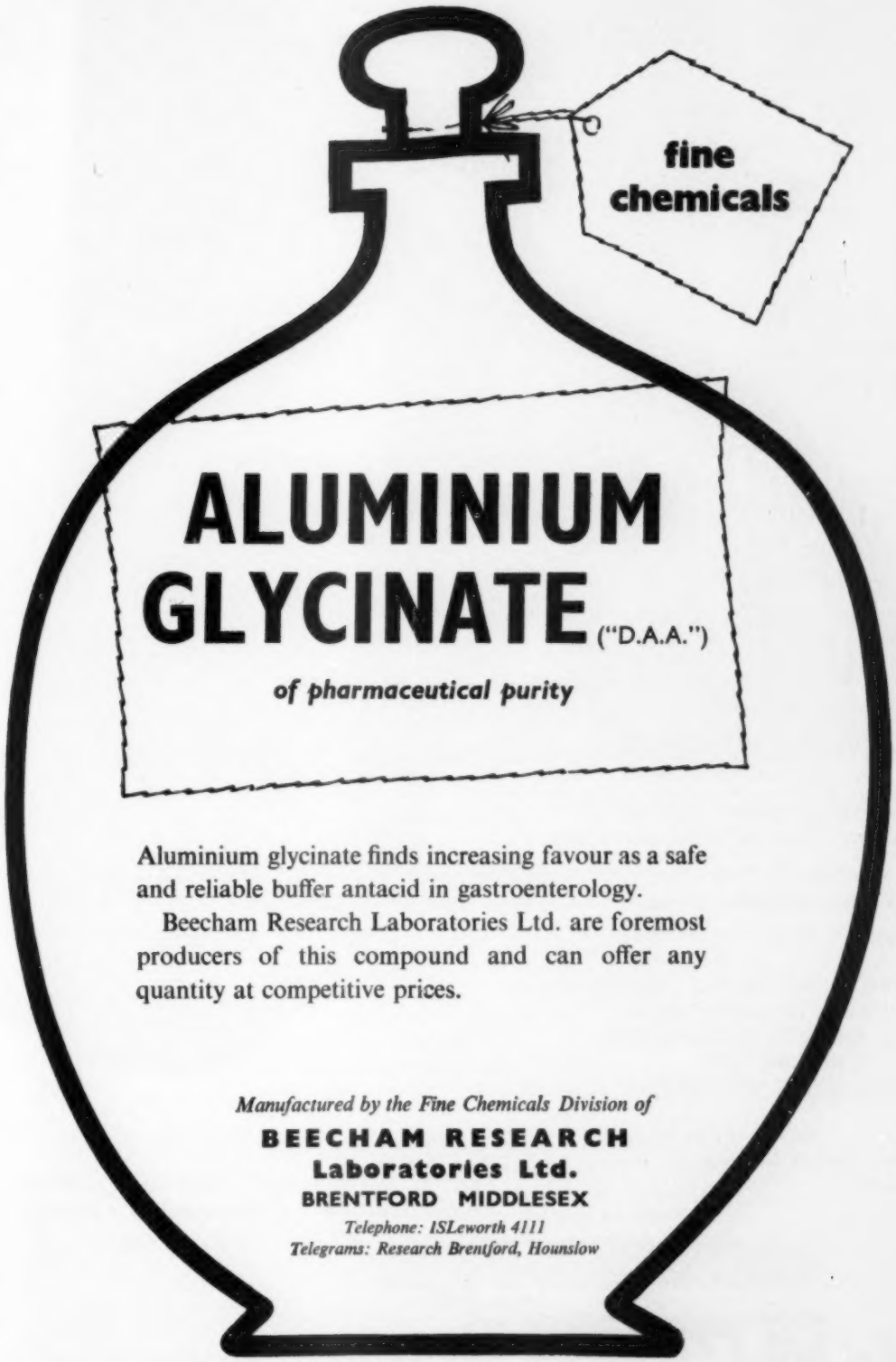

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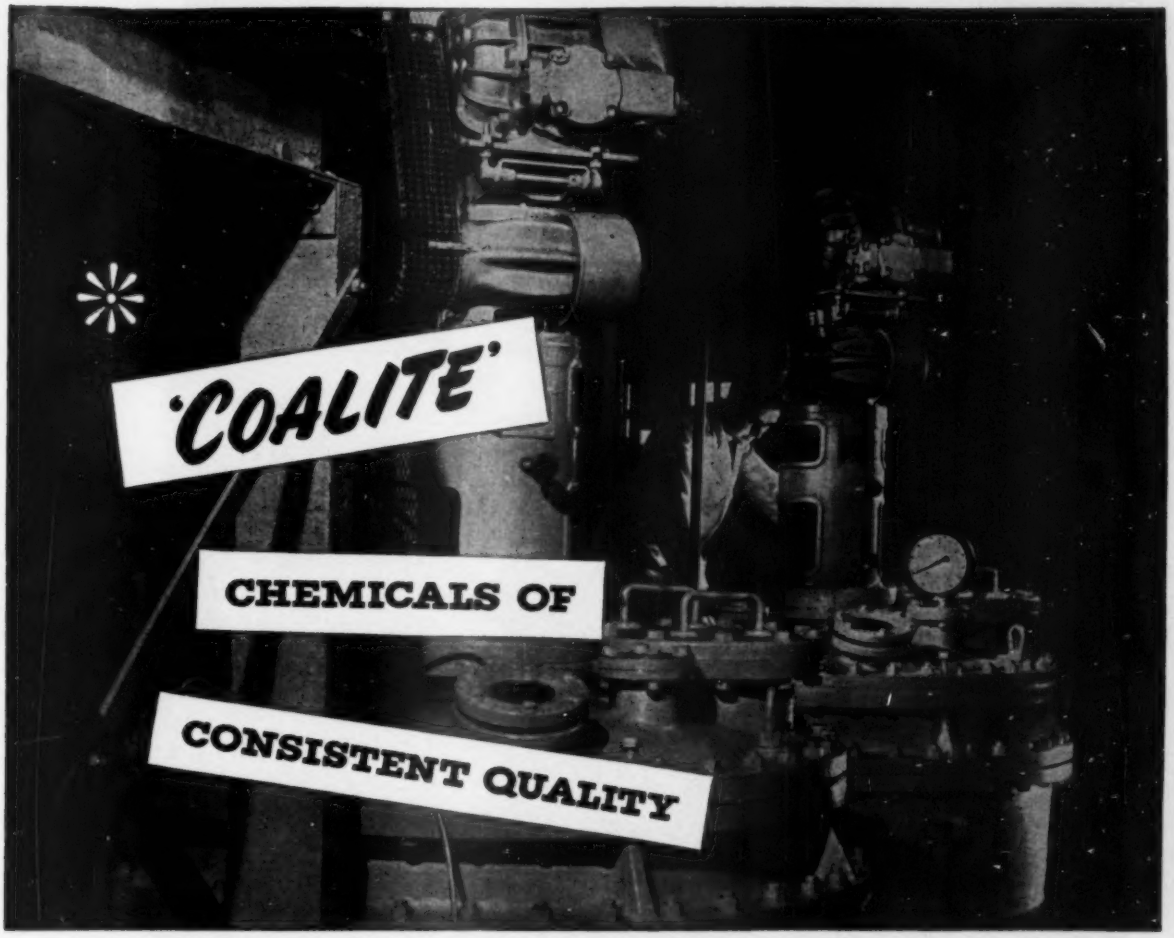

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For the removal of oxygen from other gases

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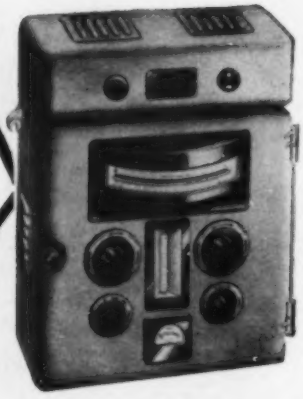

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The Hersch Oxygen Meter has been designed for the measurement of trace oxygen in other gases in the range 0-10 and 0-100 ppm. The high sensitivity, accuracy and speed of response enables this instrument to be used both for laboratory investigation and production quality control.

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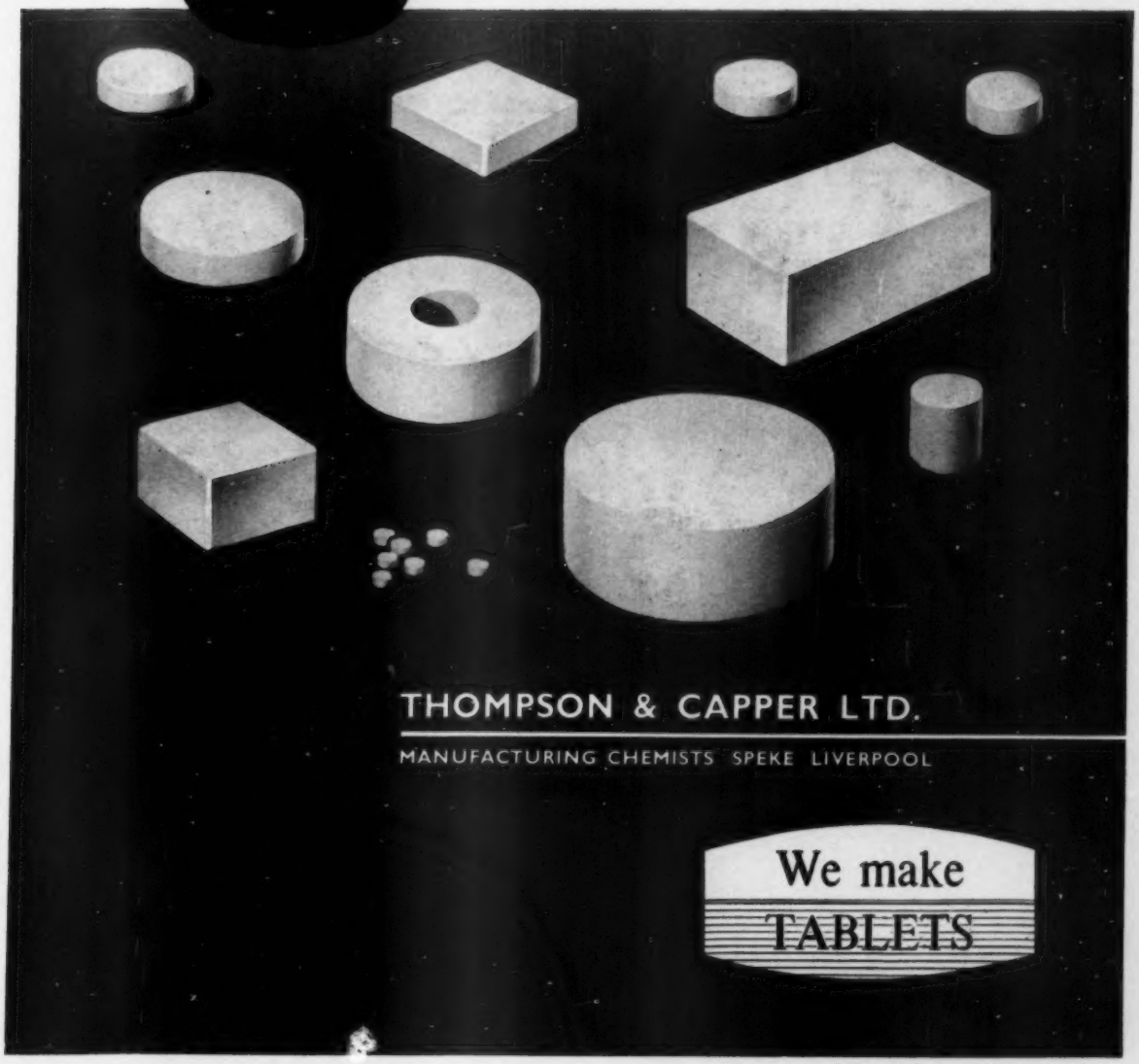

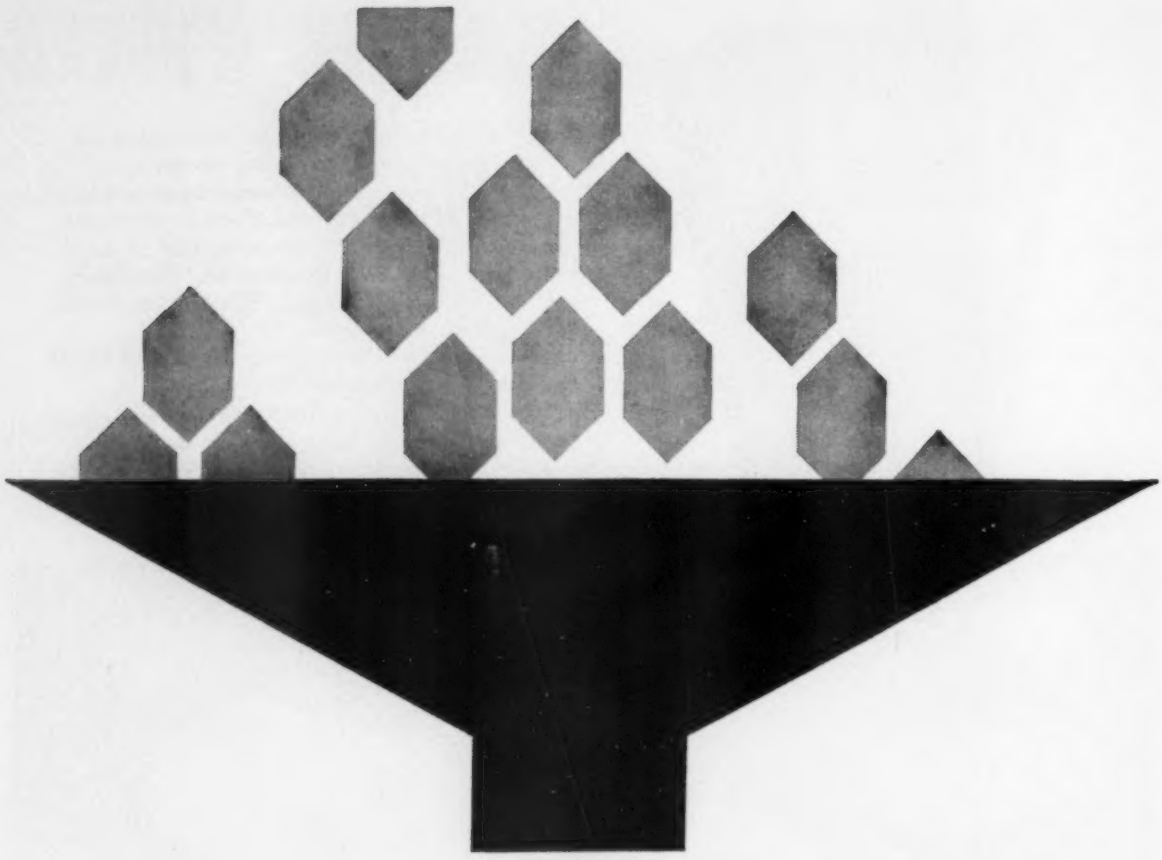

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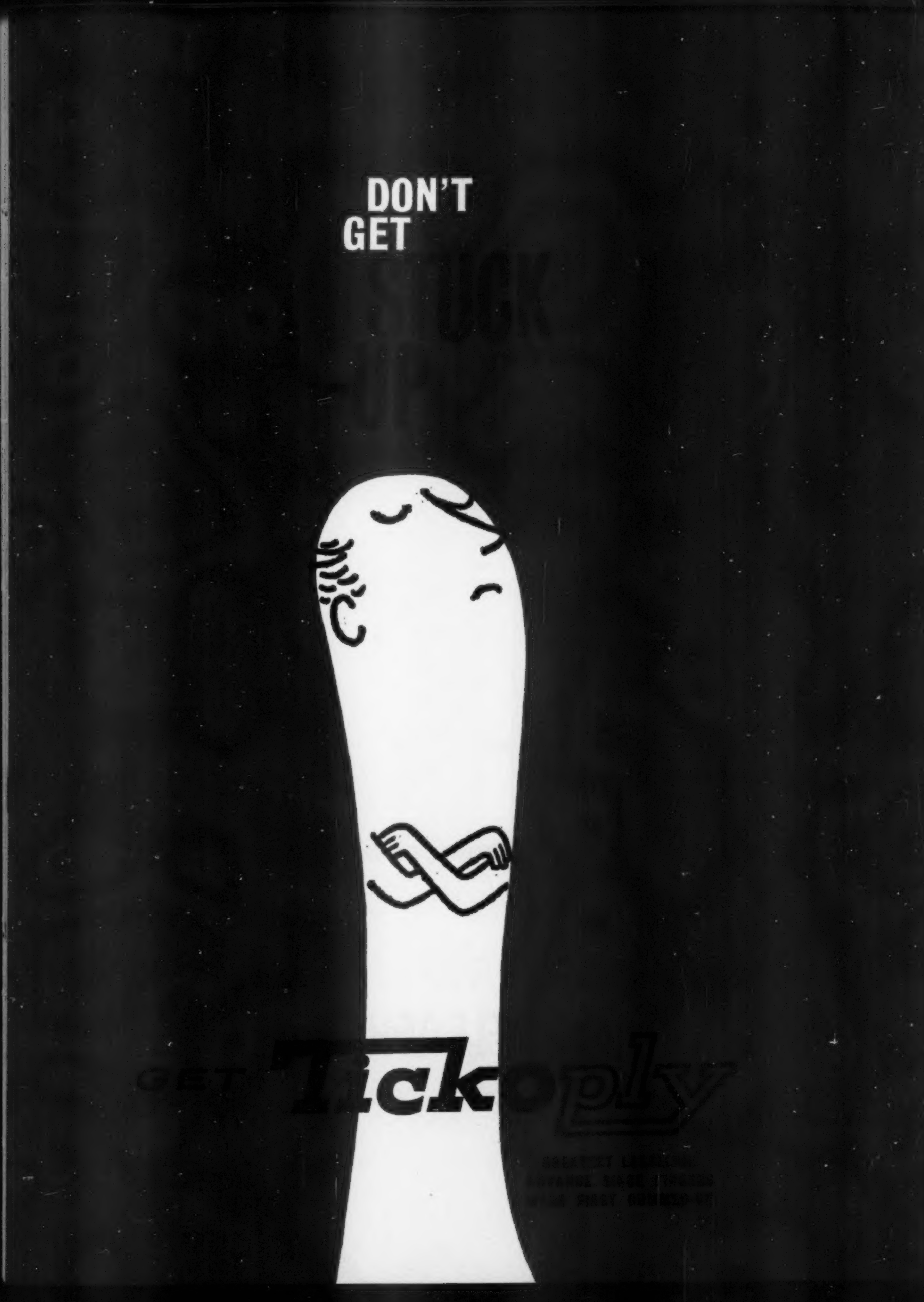
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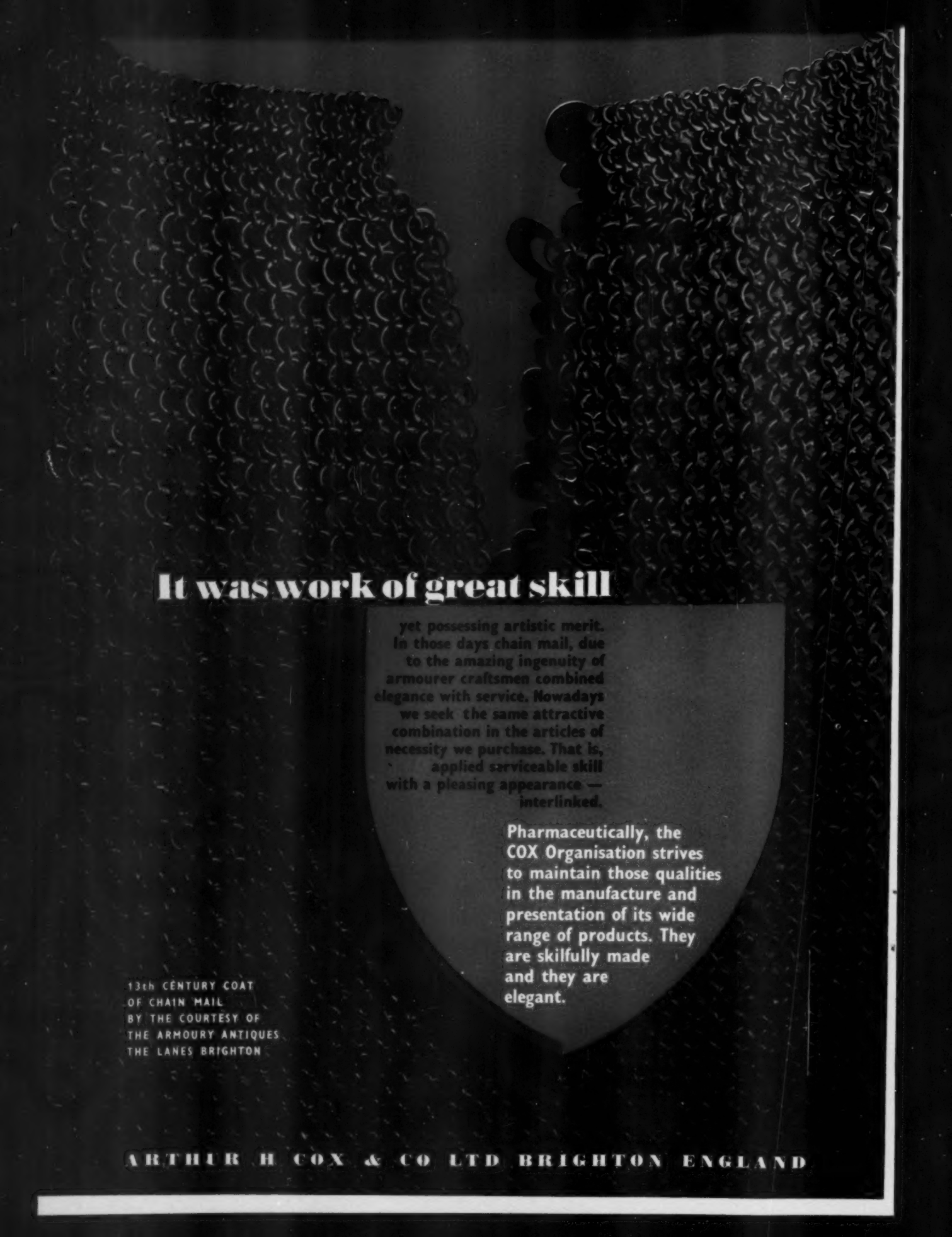

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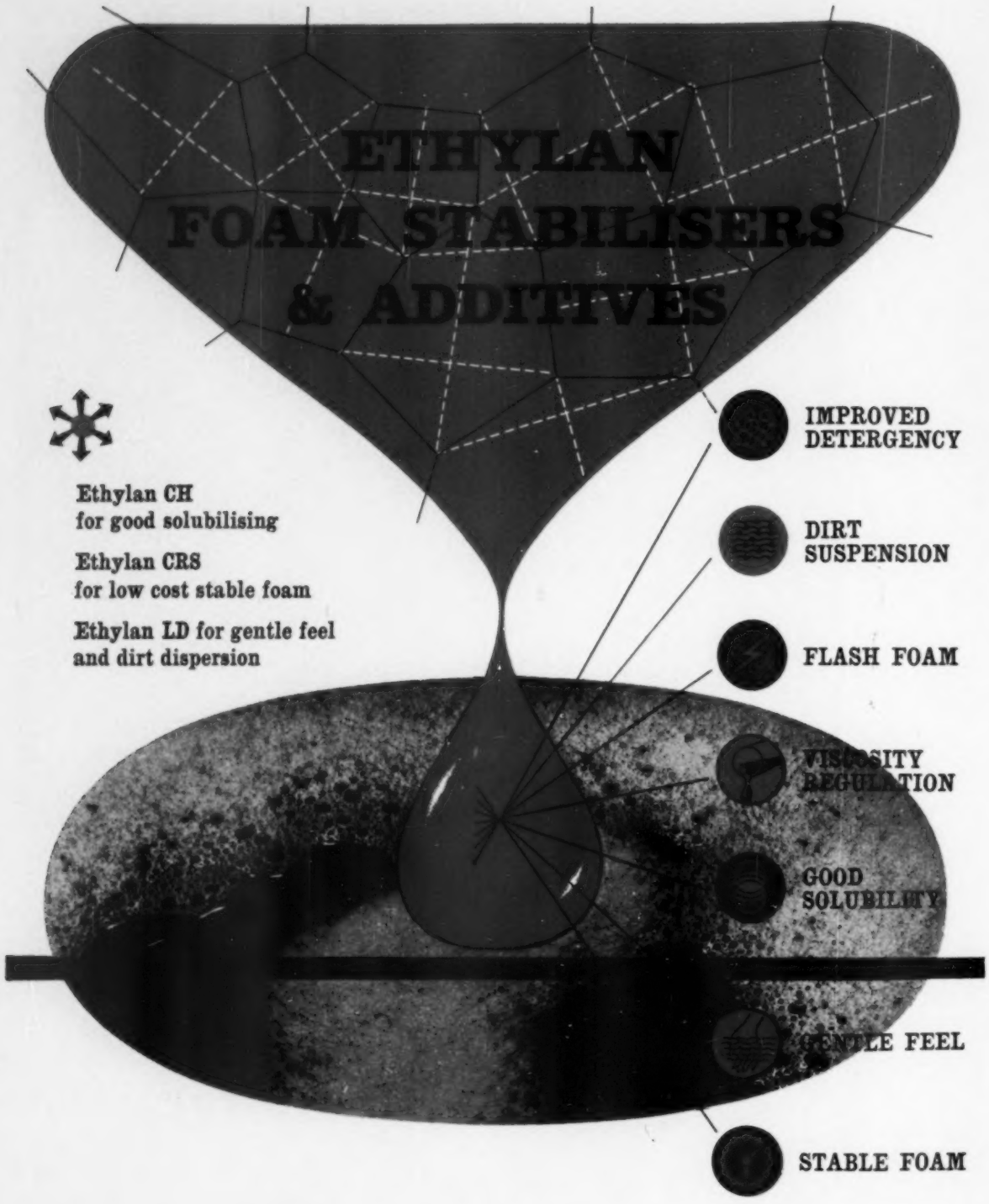

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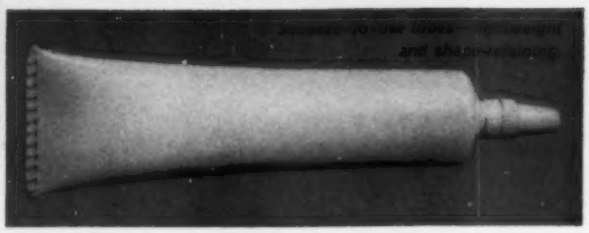

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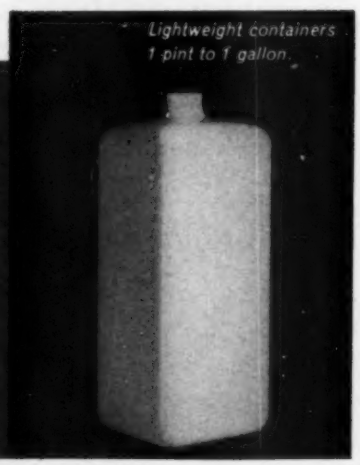

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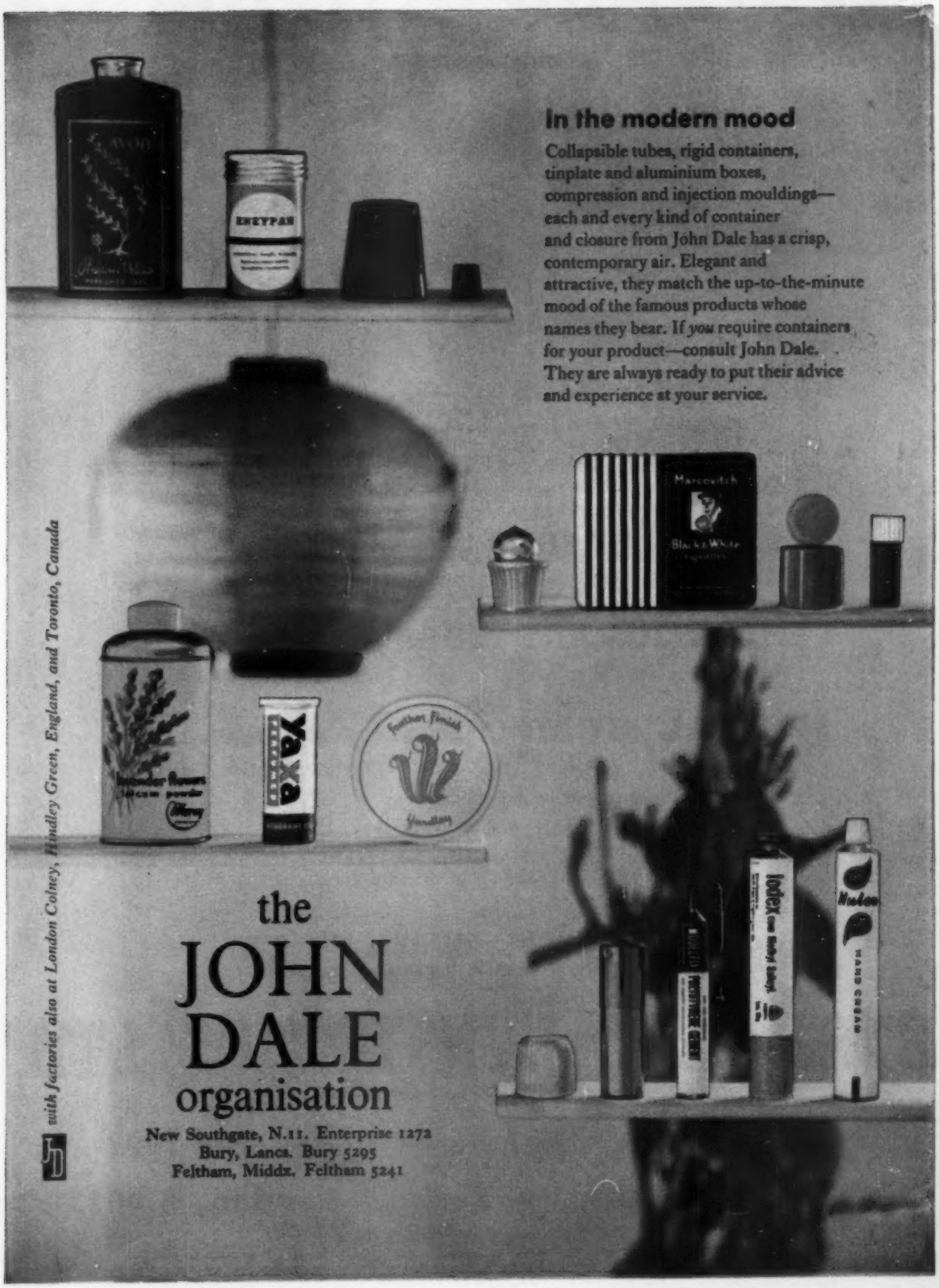
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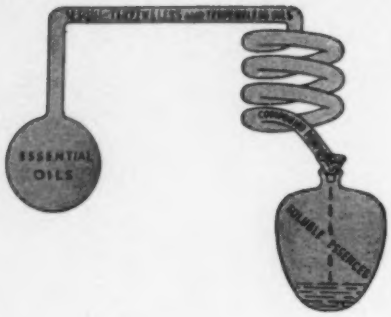

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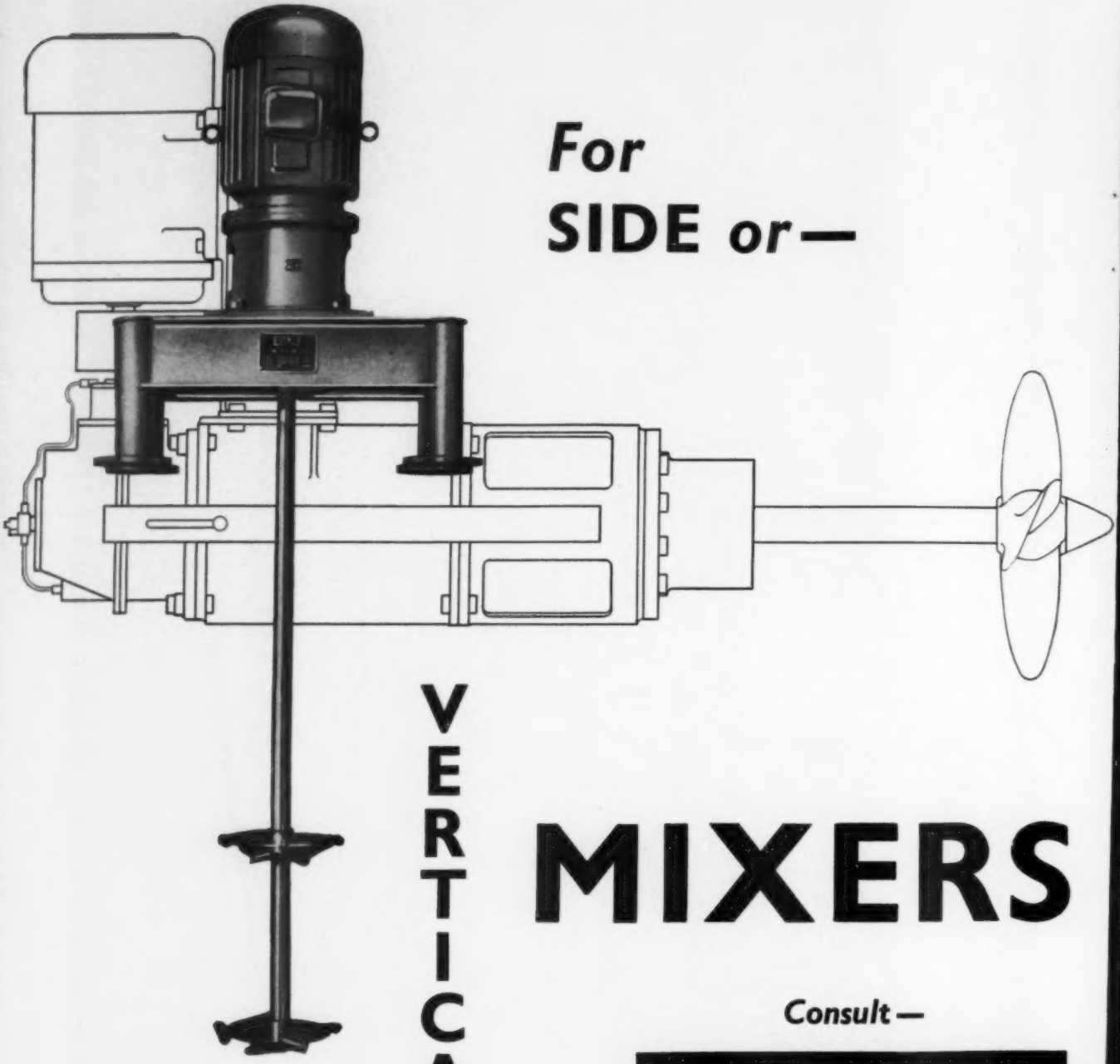


For SIDE or—

VERTICAL MIXERS

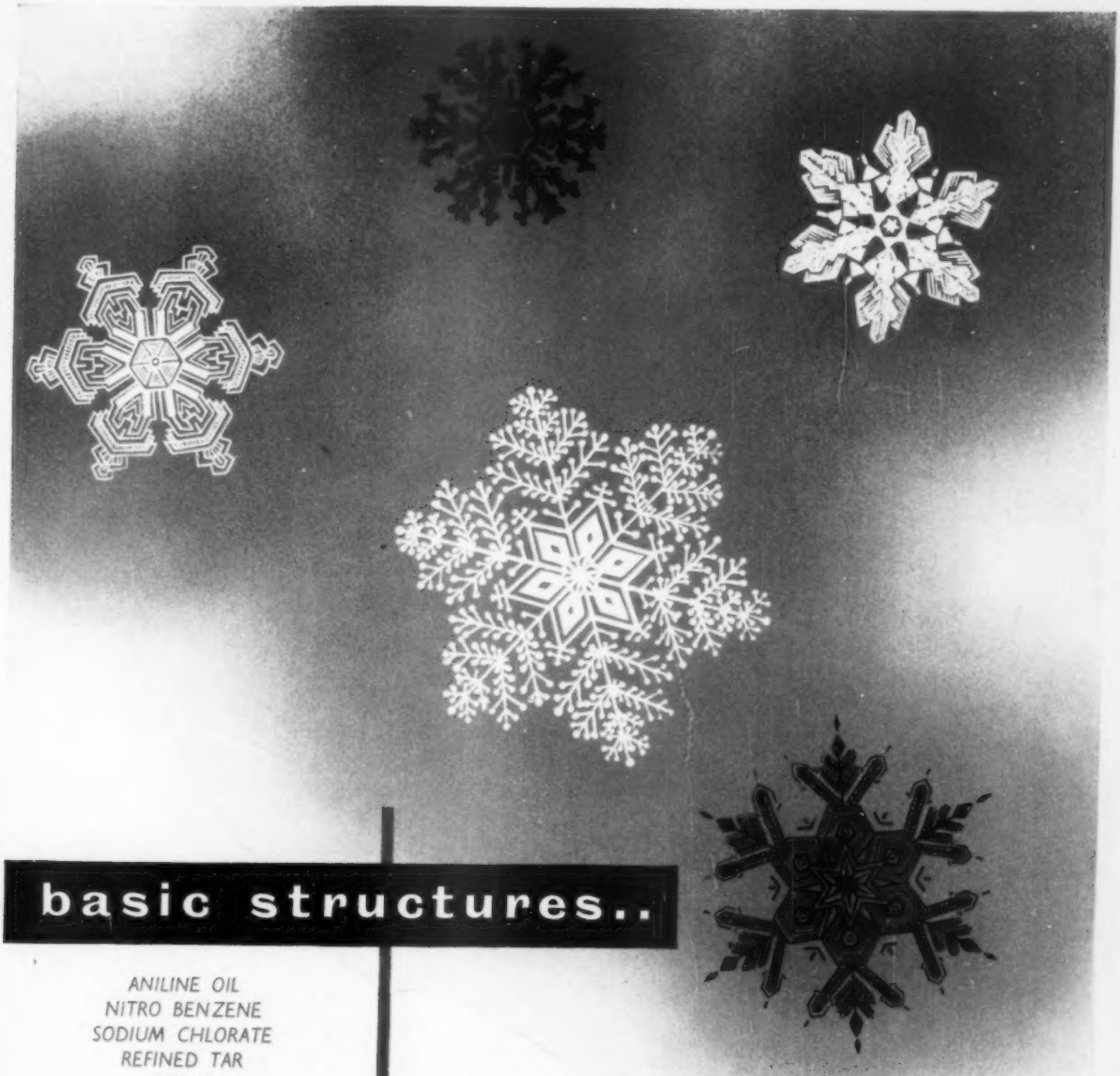
Plenty manufacture a complete range of Mixers to suit all operating conditions. The vertical unit above is of the patent "Impelator" type, a scientific design combining controlled circulation with intense mixing action. The Plenty patent, side entry, Propeller type mixer for large tanks is fitted with a mechanical seal which can be adjusted or renewed without draining the tank.

Consult—

PLENTY & SON Ltd.

NEWBURY, BERKS.

Telephone: NEWBURY 2363 (5 lines)
Telegrams: PLENTY, NEWBURY, TELEX
Telex: 84110



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. . for Nature's purposes take many entrancing forms, Stanton and Staveley Chemicals are basic to many industrial processes and their quality is maintained by vigilant control during manufacture. Stanton and Staveley ensure that supplies are on the spot when you need them. You can rely on Stanton and Staveley.

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BASIC CHEMICALS *for* INDUSTRY

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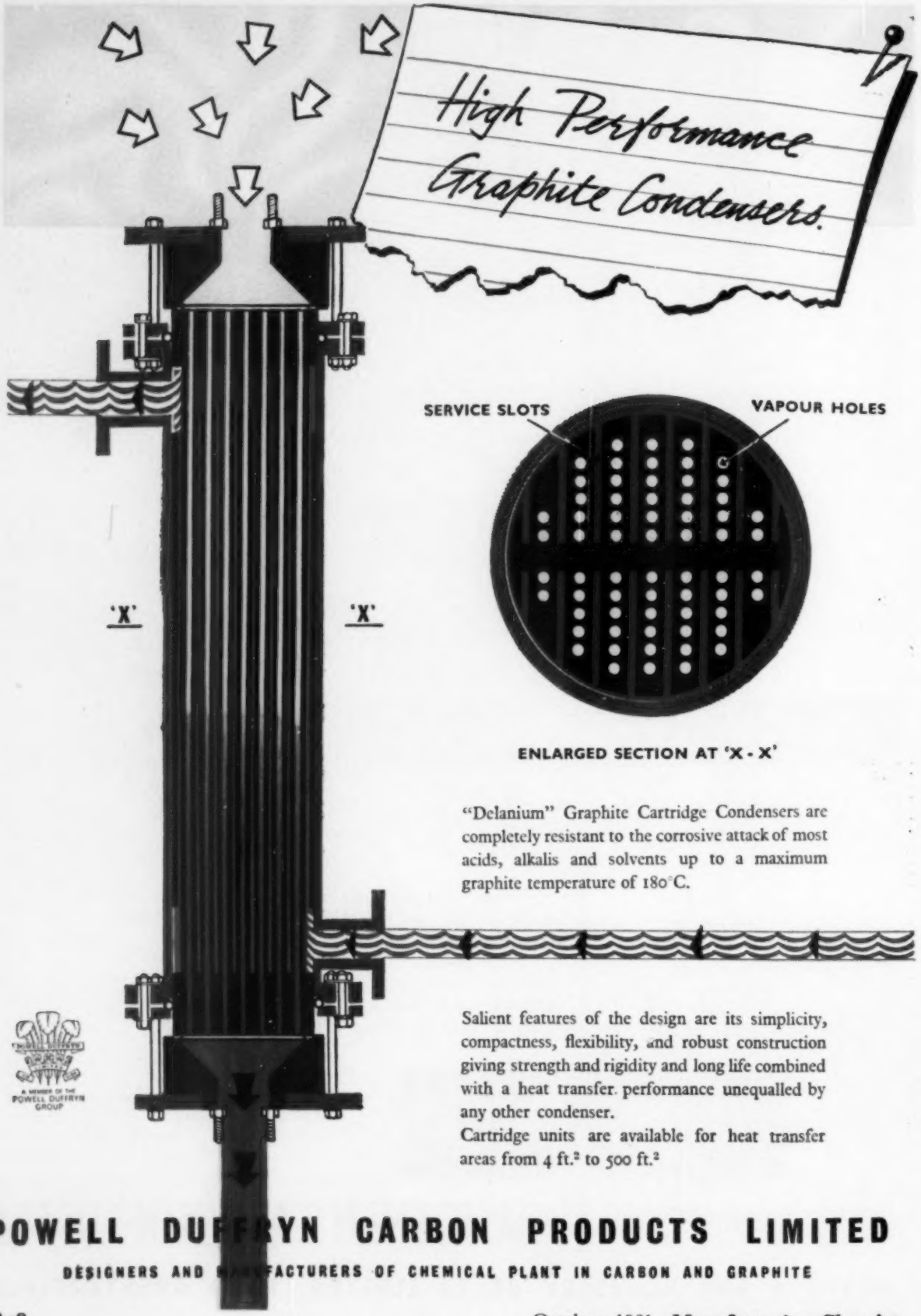

ENLARGED SECTION AT 'X - X'

"Delanium" Graphite Cartridge Condensers are completely resistant to the corrosive attack of most acids, alkalis and solvents up to a maximum graphite temperature of 180°C.

Salient features of the design are its simplicity, compactness, flexibility, and robust construction giving strength and rigidity and long life combined with a heat transfer performance unequalled by any other condenser.

Cartridge units are available for heat transfer areas from 4 ft.² to 500 ft.²

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POWELL DUFFRYN CARBON PRODUCTS LIMITED

DESIGNERS AND MANUFACTURERS OF CHEMICAL PLANT IN CARBON AND GRAPHITE

NOW!

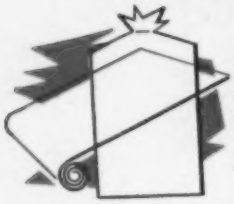
'Queensway'

Polythene Liners for the Chemical Industry

from Europe's largest maker of Polythene film

A NEW PACKAGING SERVICE You know British Visqueen Ltd. as polythene film producers (the largest in Europe), you know them as the acknowledged experts in polythene film packaging Now meet them as the makers and printers of Queensway polythene liners.

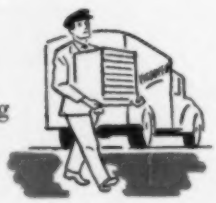
Queensway liners give you four big advantages



1. Top quality polythene film selected from British Visqueen's wide range to your specification.

3. Wide knowledge of chemical industry requirements means that your problems are quickly understood and expertly solved.

2. Prompt delivery ensured by modern equipment and really big production capacity.



4. Reliable sealing plus effective protection backed by long experience in the whole field of polythene packaging.

BRITISH VISQUEEN LIMITED

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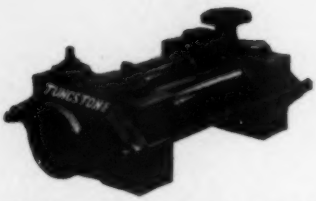
NICKEL/CAST IRON—10 sizes, 375 to 9,000 galls./hr. (Rubber lined—in 8 sizes, 800 to 9,000 galls./hr.)



EBONITE PUMP non-immersion type. Made in 3 sizes: 200, 375, 600 gallons/hour.

Troublesome Liquids need

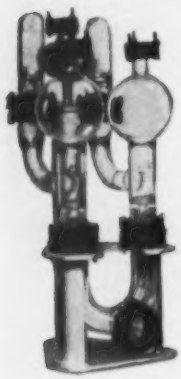
TUNGSTONE PUMPS

Which particular liquid in your business presents its pumping problem? Is it an acid, a slurry, a sludge . . . gritty greasy, corrosive, erosive, sticky? A TUNGSTONE Pump will quickly take care of that—as many industries have proved.

These fine pumps specially evolved for the handling of 'awkward' liquids have two valuable features: (a) the unit can be supplied in a range of materials which resist corrosion by any particular liquid, (b) there are no packings or glands within the unit and there is nothing to clog or choke—air is used as a piston, although it never mixes with the liquid: maintenance costs are negligible.

For any given pumping pressure the volume of air going to the pump can be controlled so that the pump's output can be varied from zero to maximum. The pump and whole length of delivery pipe containing valuable liquid can be emptied after each operation at the end of a shift.

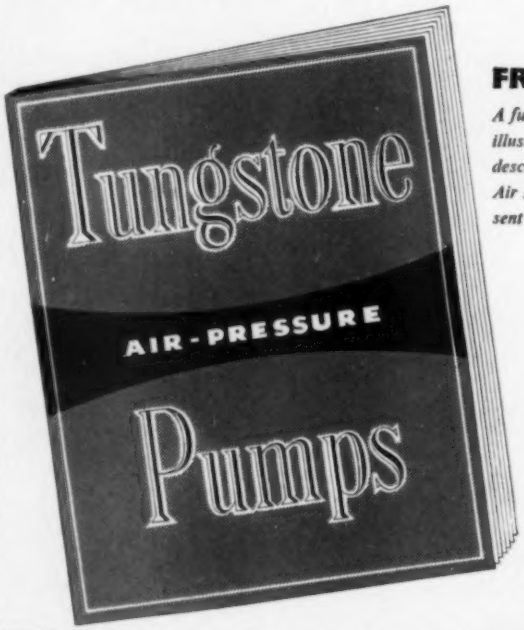
non-immersion LEAD PUMP. Made in 8 capacities: 375, 600, 800, 1,200, 1,500, 2,000, 3,000, 3,600 gallons/hour.



GLASS PUMP—"Pyrex" brand Borosilicate Glass. 300 gallons/hour.

LEAD PUMP—immersion type. Made in 8 capacities: 375, 600, 800, 1,200, 1,500, 2,000, 3,000, 3,600 gallons/hour.

EBONITE PUMP, immersion type. Made in 3 sizes: 200, 375, 600 gallons/hour.



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A fully explanatory, illustrated brochure describing TUNGSTONE *Air Pressure Pumps sent on request.*

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PASTE, LIQUID OR AEROSOL POLISH–

emulsifiable A-C® Polyethylene improves them all

Emulsifiable A-C Polyethylene, a new wax-like polymer, improves polishes of all types in gloss, ease of buffing, and resistance to water-spotting and scuffing.

In floor polishes, A-C Polyethylene stands up well in wet weather and provides anti-slip properties, often eliminating the need for anti-slip additives. To paste and solvent formulations used for cars and fine furniture, it contributes high gloss, durability and ease of application. And liquid shoe polishes containing A-C Polyethylene produce bright, lasting shines even on badly scuffed leather.

Easy, Economical To Use

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Because A-C Polyethylene is a synthetic material, it is free from problems of price and supply, characteristic of natural waxes.

Technical Literature. The new booklet "A-C Polyethylene for Polish" contains a wide range of polish formulations for floors, shoes, motor cars, furniture etc. Literature, Ref 63, samples and additional information may be obtained from the sole U.K. distributors and stockists.

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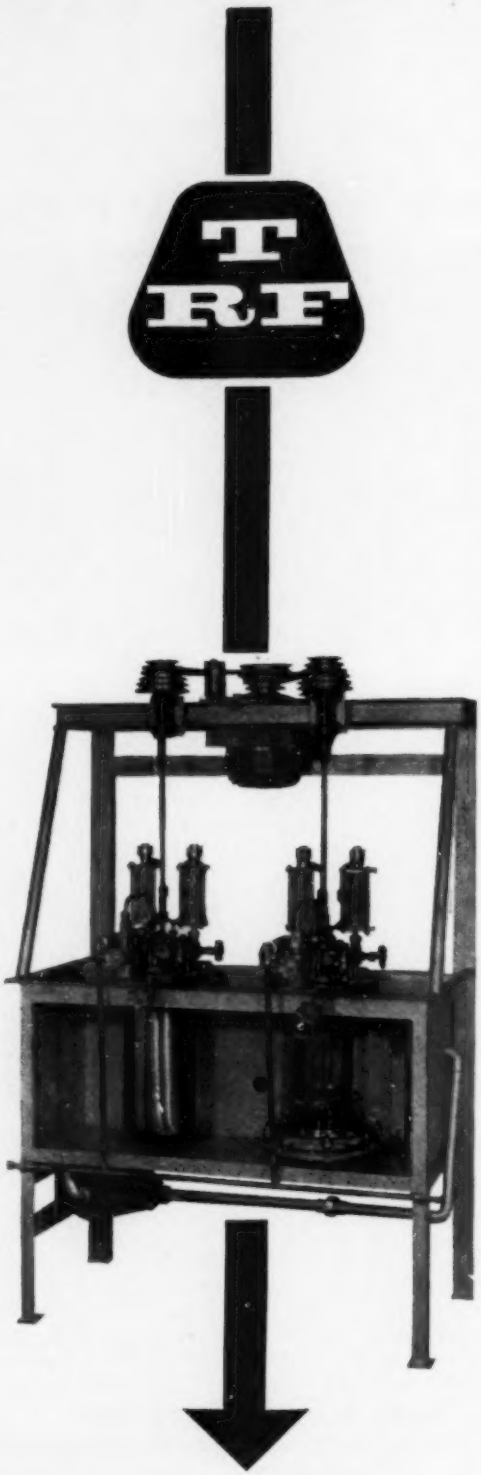
Executive Office: 40 RECTOR STREET, NEW YORK 6, N.Y.
European Office: 19 AVENUE DES ARTS, BRUSSELS 4, BELGIUM

ONE STEP AHEAD



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STACKING CONTAINERS

4 DEPTHS NOW OFFERED

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CS.24159–23½"x14½"x9½" **CS.24155–23½"x14½"x5½"**
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SPECIALLY TREATED TO GIVE MAXIMUM STRENGTH TO THE BASES.

- ★ Absolutely hygienic and easy to clean
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First Choice for Aluminium Equipment

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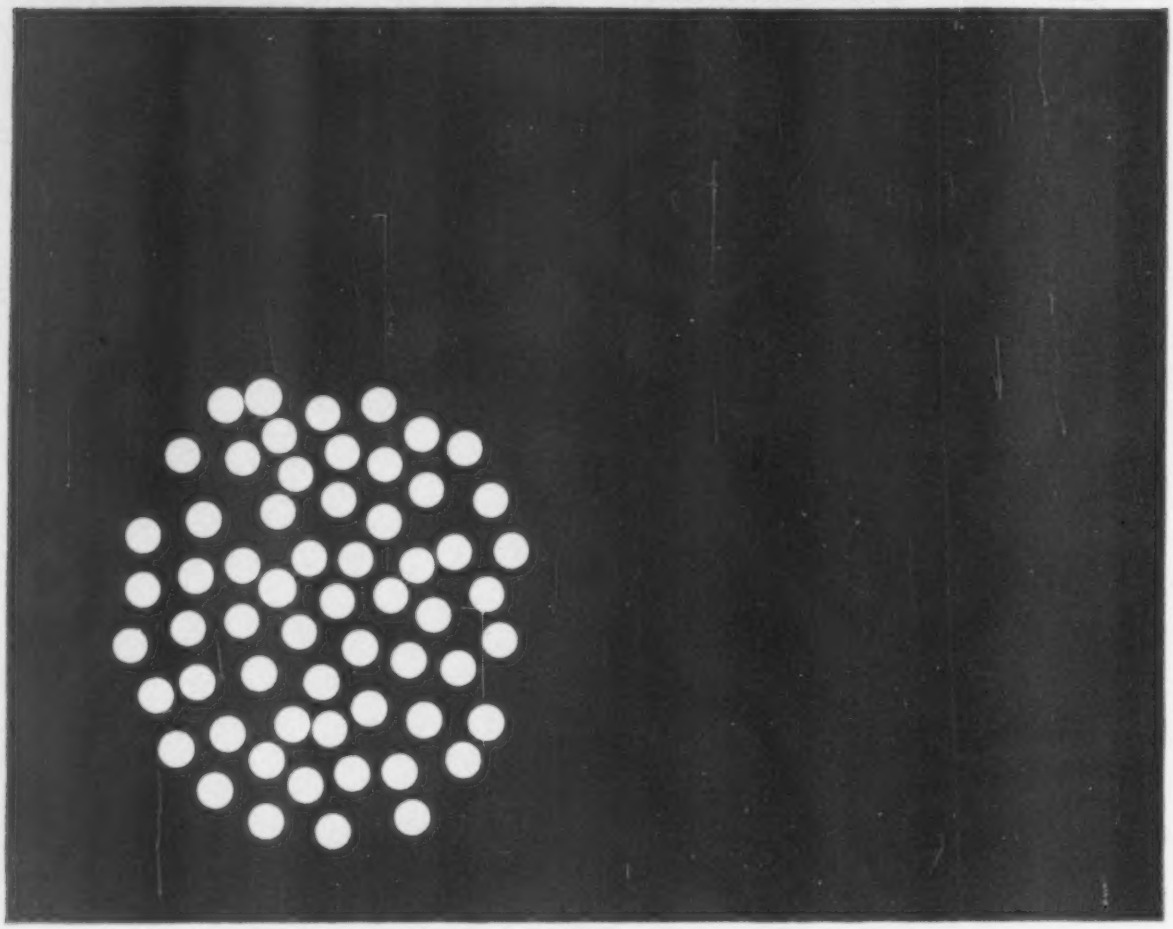
methyl cellulose ethers from I.C.I.
'Methofas' M and 'Methofas' HPM



'Methofas' M methyl cellulose and 'Methofas' HPM hydroxypropyl methyl cellulose are now being supplied by I.C.I. to meet growing demands for water-soluble non-ionic methyl celluloses as dispersing, stabilising and binding agents, adhesives and water-retaining agents in many industrial, pharmaceutical and foodstuffs applications.

For product data sheets and further information, write to your nearest I.C.I. Sales Office or to the address below.

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NC.5

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Uses Bulletin

For the preparation of shampoos for human and veterinary use, hand cleaning gels, germicidal skin cleansers — **EXONICS**, high foaming, low odour, mild surfactants compatible with most phenolic bactericides.

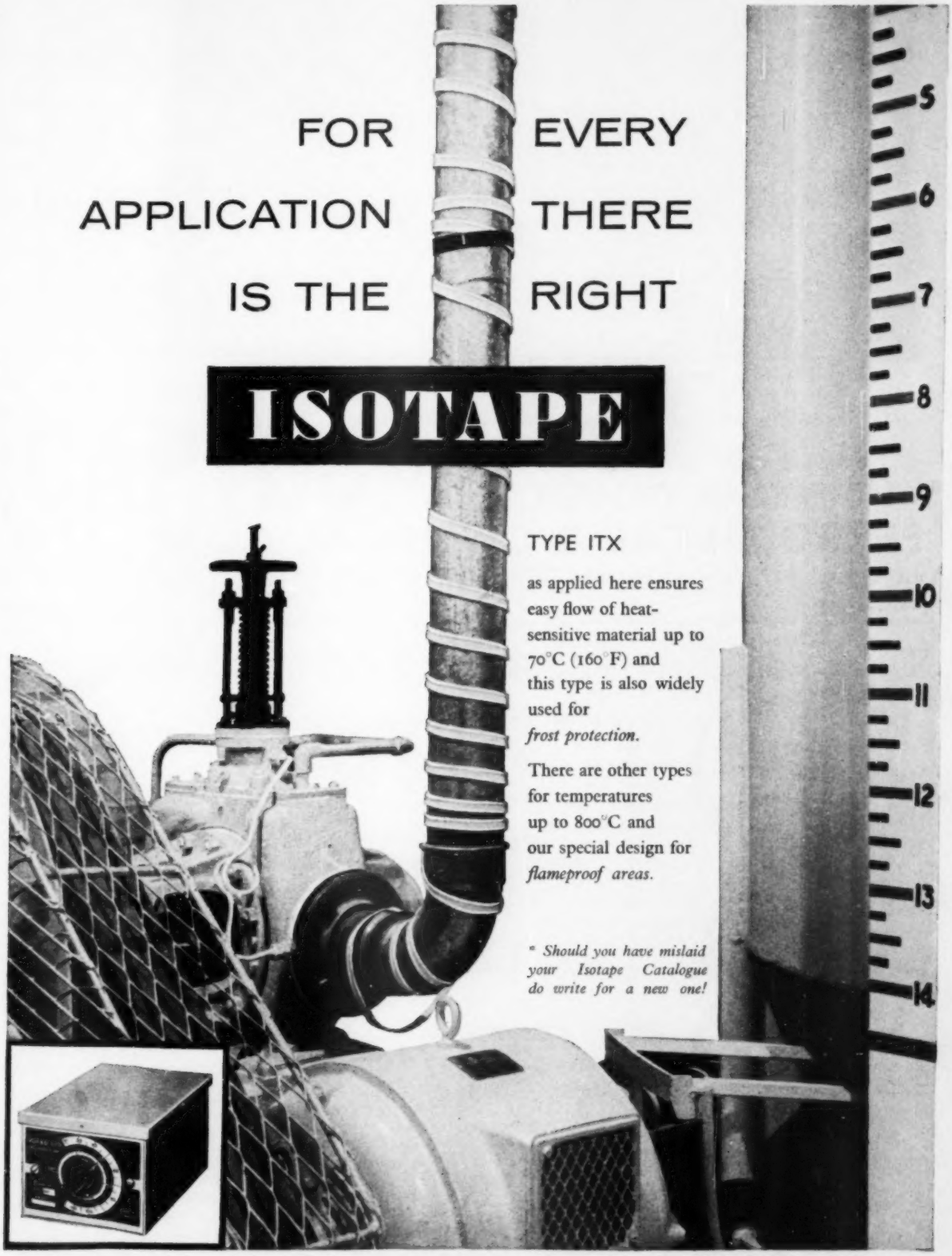
For the preparation of germicidal creams and ointments, hair conditioning creams and most cosmetic emulsions where cationic properties are desirable — **COLLONE QA** (Cationic emulsifying Wax BPC).

For use in dairy sanitisers, antiseptic lotions, sterilising detergents, germicidal sprays, etc., —**MORPANS**, a wide and versatile range of quaternary ammonium compounds.

Glovers (Chemicals Ltd., Wortley Low Mills, Leeds, 12 Telephone: 63-7847/8/9 Telegrams: "Glokem, Leeds

FOR EVERY APPLICATION THERE IS THE RIGHT

ISOTAPE



TYPE ITX

as applied here ensures easy flow of heat-sensitive material up to 70°C (160°F) and this type is also widely used for *frost protection.*

There are other types for temperatures up to 800°C and our special design for *flameproof areas.*

* *Should you have mislaid your Isotape Catalogue do write for a new one!*

Our thermostats are now calibrated in °C and °F

ISOPAD ELECTRIC SURFACE HEATERS

ISOPAD LIMITED,
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CAPTOCAP REGD. TAMPERPROOF SNAP-CAPS

Prominent pharmaceutical and food manufacturers in U.S.A., Canada and many other countries are already using these caps in very large quantities.

British manufacturers will find the following advantages of special interest:

- The cap when fitted becomes a part of the container. It cannot be opened without showing signs of interference.
- The cap is simple to open — just tear off the removable strip by pulling the lug.
- The cap is captive, attached by a hinge to the clamping ring. It snaps shut providing a perfect closure throughout the life of container.
- The cap is suitable for all types of glass containers —bottles, jars and 'Trident' tubular vials.
- The cap may be used for pharmaceutical products, foods, soft drinks and for many other purposes.
- The cap is made of polythene. It is hygienic, non-corrosive, impermeable and unbreakable. Supplied in natural or coloured polythene, embossed if desired.
- Neck rings for bottle to accommodate the caps can be made at low cost to fit existing bottle moulds.
- Prices are competitive with normal capping and sealing processes.

We are the manufacturers of CAPTOCAP Tamperproof Snap-caps and the Sole Licensees for their use with glass containers in Great Britain. Write for our illustrated leaflet.

FITTING. CAPTOCAP Tamperproof Snap-caps are easy to fit by hand operated, semi-automatic or fully automatic machines. Existing capping machines can be adapted in some cases. We shall be pleased to advise manufacturers about their existing plant, or supply information regarding special machines.

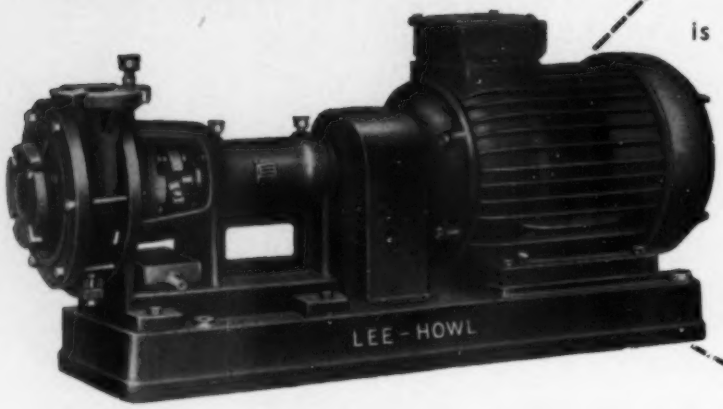
JOHNSEN & JORGENSEN LIMITED

30 ST. BRIDE STREET, LONDON, E.C.4

Tel: LUDgate Circus 0701 (8 lines)

WHAT IS A . . .

"HYPERSILID" PUMP?



The Lee-Howl "Hypersilid" is a Horizontal, End Suction, Centrifugal Pump, with open type impeller. It will handle corrosive liquors, sulphuric acid, nitric acid, acetic, formic, phosphoric, etc.

The pump is made in the works of Lee, Howl & Co., Ltd. of Tipton, from Silicon Iron castings manufactured by Bradley & Foster, Ltd. of Darlaston, in collaboration with whom it has been specifically designed.

LEE, HOWL & CO., LTD.

London Office:
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FINCHLEY, LONDON, N.3.

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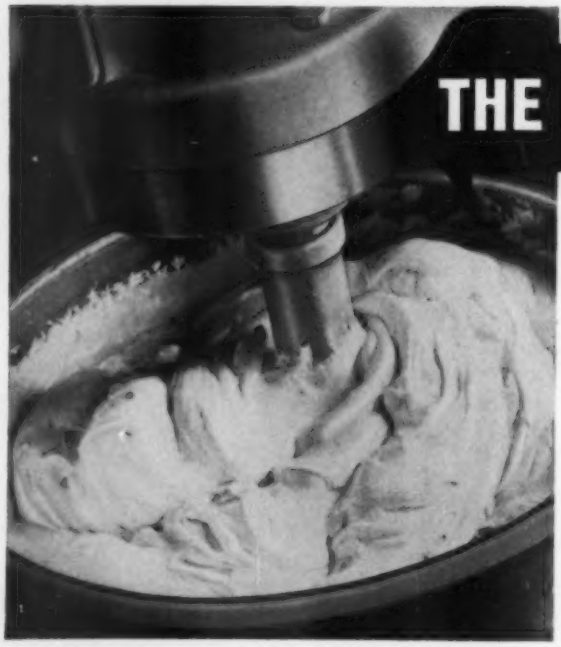


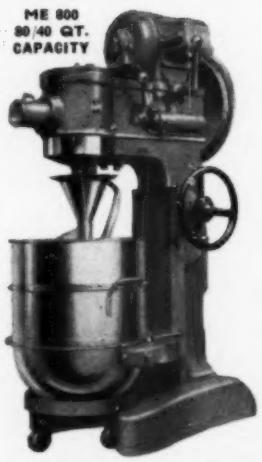
THE ULTIMATE IN MIXING

If you need a perfect mix, and an unfailingly reliable machine to produce it—you need a Hobart Mixer.

Hobart Mixers, electrically powered, have a unique planetary action with an epicyclic movement. Outstandingly efficient, their range of speeds and their variety of mixing tools make them ideal equipment for the Cosmetic and Pharmaceutical Industries.

There are seven models—bowl capacities 5 to 140 quarts.

Please write for full details of them.



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Bedford-Hawson 3 ton Box Van!

670 CUBIC FT CAPACITY

Body 670 cu. ft.—modern looking—practical. With sturdy construction and a 10-gauge steel underframe and hardwood floor. Built by volume production methods for a price of only £281.

Chassis Low-loading, low-priced Bedford chassis, with the famous cab-ahead-of-engine TK design, giving easy access, walk-through floor, sound-proofed comfort and superlative vision. Complete vehicle price, with 214 cu. in. petrol engine, £1,106; with 200 cu. in. diesel £1,226. Same body also available on TK 4 ton or 5 ton 135 in. wheelbase chassis.

Plus The unmatched advantages of Bedford's years of practical experience and technical know-how in the transport vehicle business. A product of the largest commercial vehicle factory in Europe.

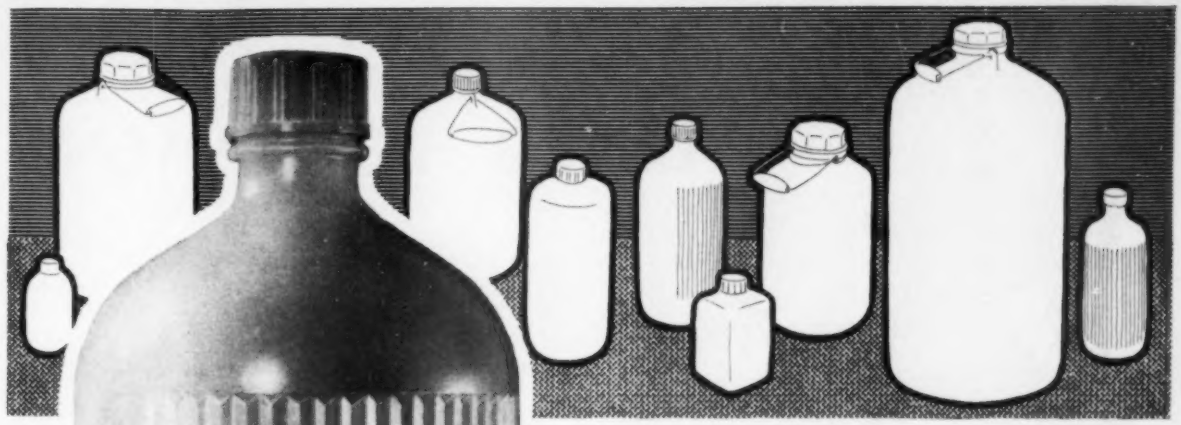
PRICE COMPLETE

£1,106

Full details of this outstanding new van from your local Bedford dealer.

Better buy BEDFORD

Vauxhall Motors Ltd., Luton, Beds.



...extending an already FAMOUS range of SELLERS

THE Freeflex

90 OZ.

HALF RIBBED Blown Polythene Container

Being of Winchester size, half-ribbed and closed with a 38 m.m. high-density polythene cap fitted with "Suba-Rite" washer, it is particularly suited as an easily-handled container for poisonous and corrosive liquids, and thus forms a most useful counterpart to the standard "Freeflex" 90 oz. bottle. It is available in low- or high-density polythene.

STRONG, LIGHT, UNBREAKABLE!

"Freeflex" Blown Polythene Containers, which are all available from stock, range from 5 c.c. to 5 gallons capacity. The 1 and 2 Gallon sizes are available in narrow or wide necks, and with or without carrying handles, as required. If you deal with Heavy or Fine Chemicals, Pharmaceuticals, Paints, Varnishes, Dyes, Waxes, Powders etc., you can lighten your shelves, your labour and your packaging problems by cutting your container weight more than 70% with "Freeflex".

Write for sample and details to-day.
You may also care to have information about our wide series of "Suba-Seal" Closures in rubber and other materials to meet your every need in this field.

WILLIAM FREEMAN & CO., LTD., SUBA-SEAL WORKS, STAINCROSS, BARNSLEY, YORKSHIRE.

GLASS ENAMEL LINED EQUIPMENT

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A Complete Plant or a Single Unit.

Designed to meet your own requirements, and lined with a Hard Glass Enamel developed during over a century of service to the chemical industry.

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HIGH-SPEED AUTOMATIC BOTTLE FILLING PLANT

THE ROBERTS "STRAITLINE"

MULTIPLE HEAD VACUUM FILLING MACHINE

Nº 714

- FITS CONTINUOUS PROCESS LAYOUTS
- VARIABLE SPEED AND BOTTLE SIZES
- ALTERNATIVE VACUUM OR VACUUM PLUS GRAVITY FILLING AS INITIALLY REQUIRED
- EASY CLEANING—CLEAN FILLING—HIGH SPEEDS
- FLOAT CONTROLLED LIQUID STORAGE TANK ENCLOSED

ROBERTS PATENT FILLING MACHINE CO. LTD.

BOLTON · ENGLAND

Phone: Bolton 4925 (2 lines).

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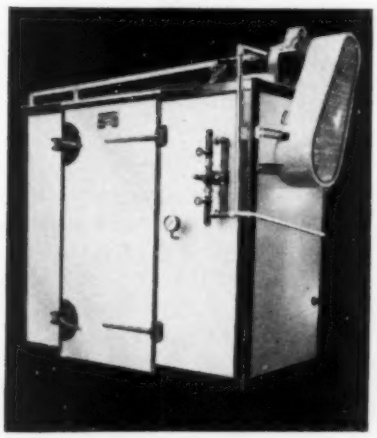

A Briggs single truck oven—one of the many steam, electrically and gas heated drying ovens in the Briggs standard range.

Keeping dry and getting dried out are, of course, two entirely different things.

And we think it is worth pointing out right away that neither are even remotely similar to the science of controlled drying as it is understood—and understood very well—at Briggs.

We have perfected a wide range of standard drying ovens which are sufficiently versatile to solve the difficulties of almost every manufacturer who has a drying problem. Standardisation, as all the best captains of industry will tell you, brings economy in its wake—and that means that Briggs drying equipment is not only better, but cheaper.

At this point we have no wish to go all technical, as doubtless many readers are anxious to pass on to the other interesting advertisements in the paper; but before leaving us it is worth noting that we employ a very competent technical staff who are fully qualified to answer any queries you may have, and to advise on the best kind of drying equipment to install in those rare instances where specially designed ovens are required.

THE SPECIALISTS IN COMPLETE DRYING PLANT

BRIGGS
OF BURTON

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MIXING

is a BIG word at Gardners

Whatever the material you require to be mixed, it is almost certain that Gardners can provide a suitable machine for the job.

They supply Mixers of various types from 15 lbs to 30 tons capacity, and ancillary plant to go with them.

Whatever your mixing problem . . .

Talk to

GARDNERS *of Gloucester*

Wm. GARDNER & SONS (GLOUCESTER) LTD., BRISTOL ROAD, GLOUCESTER

(A subsidiary of the Gloucester Railway Carriage & Wagon Co. Ltd.) Phone: Gloucester 21261
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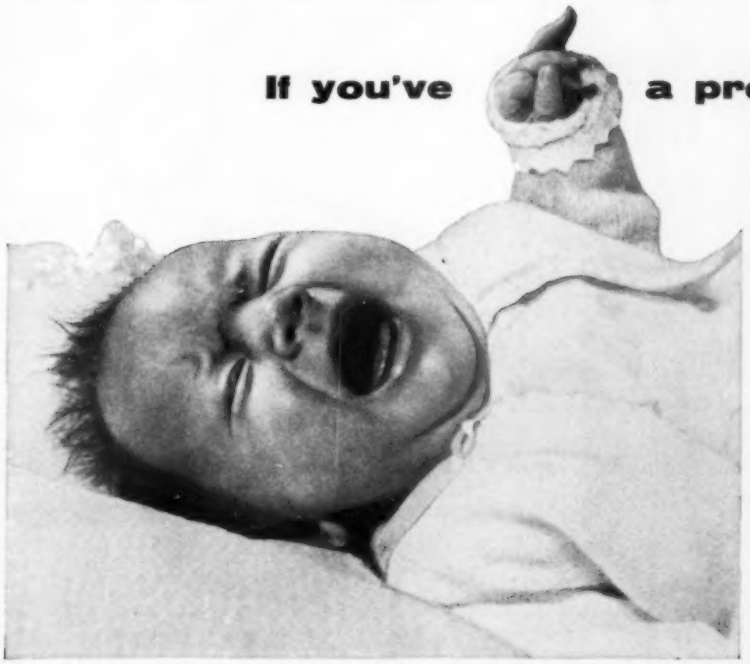
THE AIRMIX

Mixes powders 10 times faster !

Air blasts through the mixing head at the base of the machine agitate the powder in a spiral action which gives a perfect mix. There are no blades or agitators to maintain, wear out, or clean. The Airmix can be modified for use as a combined mixer and sprayer to enable liquids to be mixed with the powder. Available with working capacities from 2 cu. ft. up to 800 cu. ft.

Send for illustrated folder of the Gardner range of machines

If you've a problem child . . .



. . . that's simply crying for a spanking good injection-moulded component, let our design unit nurse it along a bit. They'll soon have it safely buttoned up.

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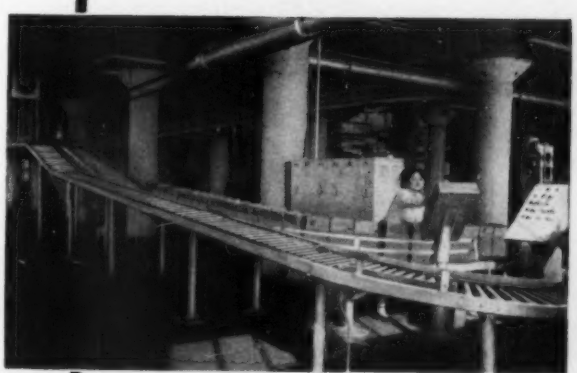

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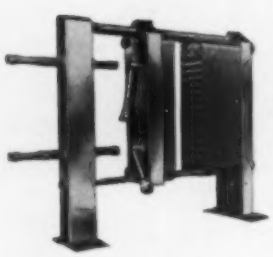

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Topics and Comments

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Pipework—neglected but vital

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It is shocking to find in a nation of so-called merchant adventurers such a depressingly supine attitude to exports. The success of Germany is not taken as a challenge but with resignation.

Managing directors of exporting companies found they could easily get export information, that the Board of Trade was helpful and that lack of foreign languages, while not exactly helpful, was not a barrier. Their counterparts in the non-exporting firms gave exactly these reasons for not bothering with exports. It is clear that in many cases it is not that a firm cannot export, but simply does not want to.

Of course if a firm can sell easily at home it needs a big effort to start into exporting. The frightening fact that the non-exporters ignore is that if the home market declines it will almost certainly be a consequence of a world recession which will simultaneously close the door to exports. If it is left too late a firm will not be able to weather a depression by turning to exports.

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2,2-Dimethyl propyl chloride
Dimethyl sulphone
Dinitro durene
n-Dotriacontane
Embelin
(see page 400 of Merck Index 7th)
2-Ethanol pyridine
N-Ethyl phenothiazine
Ethyl t.-butyl carbonate
Heptanediol-1,7
Hexahydroindane (cis/trans)
n-Hexatriacontane
2-gamma-Hydroxy propyl pyridine
3-gamma-Hydroxy propyl pyridine
4-gamma-Hydroxy propyl pyridine
Isophthalic acid (= meta-phthalic acid)
Isopropylcyclohexane
2-Methyl-5-aminohexane
3-Methyl butene-1 99%
2-Methyl cyclopentanone
2-Methyl heptane
1-Methyl heptylamine-1 (=2-Octylamine)
2-Methyl hexane
4-Methyl hexene-1 99%
5-Methyl hexene-1 99%
Methyl hydrogen adipate
Methyl 2-hydroxycyclohexane carboxylate
2-Methyl imidazole
Methyl t.-butyl carbonate
2-Methyl thiophene
4-Nitrophenylazo-4-benzoyl chloride
N-n-Pentyl succinimide
n-Octacosane
B-Phenyl ethyl mercaptan pure
n-Propyl cyclohexane
2,3,5,6-Pyrazine tetracarboxylic acid
Seleno-urea
Sodium Laevulate 95%
Sphingomyelin
Stearolic acid
n-Tetracosane
2,3,5,6-Tetramethyl-4-nitro aniline
Tetraphenyl methane
p-Thiocyanophenol
Trimesic acid chloride

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Bingo!

IT HAS always seemed to us baffling that a product so basically necessary as washing powder should require so much advertising to sell it.* And not only advertising; every kind of eye- and ear-catching gimmick too. So it really is not surprising that the latest national craze, the moronic game called Bingo, should have been used to sell detergent. Bingo is just the new name for a game at least 2,000 years old, which is variously called tombola, housey-housey, etc. It is a simple numbers-game and Thomas Hedley adapted it to sell *Daz* by printing a set of numbers on the packet and putting a slip bearing another set of numbers inside. If the numbers coincided the buyer won a prize. The effect on Bingo-crazed housewives should have been terrific. It was, but not in the way intended. Apparently women bought a packet, took out the slip inside and then searched over the rest of the packets in the shop until they found one with matching numbers. Like this they could win every time. Hedleys hastily dropped the idea while they were still solvent.

*p*H revised

THE use of *p*H as a measure of acidity and alkalinity has been established so long in science and industry that most chemists will have forgotten that originally *p*H was intended to denote $-\log_{10} C_H$, where C_H is the hydrogen ion concentration. It is now realised that this quantity is not measurable. In fact, if *p*H is to be a measurable quantity it cannot have any exact simple fundamental significance. It is therefore necessary to define *p*H in terms of the method of measurement, and since more than one definition is possible on this basis there is need for a standard *p*H scale.

In British Standard 1647, which was first published in 1950 as a result of an initiative by the Royal Society, the plan adopted is to define the difference in *p*H between two solutions in terms of a specified electrometric measurement and to complete the definition by assigning a value of *p*H at each temperature to one chosen solution, termed the *primary standard*. The definition applies to aqueous solutions within certain limits of temperature, and is intended to ensure that, when different workers refer to a stated measured value of *p*H, they mean the same thing within $\pm 0{\cdot}005$. Within this degree of accuracy there is no practical difference between the British Standard *p*H scale and the scale adopted by the National Bureau of Standards (U.S.A.), although the latter specifies four standard solutions instead of one. The primary standard specified in B.S. 1647 is a 0·05 molar solution of potassium hydrogen phthalate.

No basic change has been made in revising this British Standard, but its usefulness has been increased by extending the range of temperature covered. Originally 0-60°C., this range is now 0-95°C. Corresponding extensions have been made to the relevant tables in the Appendices.

As in the previous edition, recommendations for the use and calibration of the glass electrode are included, together with information on the *p*H values of aqueous solutions suitable for this purpose. It has not been found possible to make more than one addition to the list of these solutions, the *p*H values of which must be known reliably to an accuracy of $\pm 0{\cdot}005$, and the desirability of further additions is emphasised in the text.

Copies of this Standard (1647 : 1961) may be obtained from the British Standards Institution, 2 Park Street, London W.1, at 4s. 6d. (postage extra to non-subscribers).

Nicotine pros and cons

A CURIOUS reminder of the 400th anniversary of the coming of tobacco to Europe appeared recently in the newspapers. One of the French rebel leaders in Algeria was Jean Nicot, chief of the French Air Force, who was imprisoned for his part. The name brings back the strange story of that other Jean Nicot (no relation) who championed tobacco or *Nicotiana tabacum*, as it was later called in his honour. As French ambassador to Portugal he met the botanist De Groes who showed him a tobacco plant and gave him a few seedlings. The plant was reputed to be a cure for cancer, and a panacea which worked wonders with stomach cramp, ulcers, asthma and coughs when the leaves were plastered on the affected spot, not dried and smoked! Nicotiana thus became *L'Herbe du Grand Prieur*, Nicot being concerned only with its alleged medical uses, including the sniffing of the powdered plant to cure headaches.

From being thought a cure for cancer tobacco is now considered a cause of cancer. To the layman nicotine is a dark tarry stain, not the volatile colourless substance which is true nicotine. As a pesticide it has won full favour; 5 million lb. is produced annually from tobacco wastes. As early as 1690 this beneficial application of nicotine for combating the "pear lace bug" appeared in France.

Though Pictet and Rotschy described a synthesis of nicotine in the *Berichte* in 1904, a large-scale commercial synthesis has failed to appear. After 400 years the perpetuation of Nicot's name continues, perpetuation good or bad according to what views of nicotine are held. A few points to conclude the story. One is that the lævoform of nicotine is three times more toxic than the dextroform. A second is that Nicot's name forms part of beneficial nicotinic acid, a vitamin formed from the oxidation of nicotine, yet one which is no excuse for heavy smokers. As a laconic chemist put it, while one drop of nicotine on a dog's tongue will kill it, a few grains of nicotinic acid will save a dog's life—that is, another dog's.

* Readers similarly puzzled should read Hedleys' statement on advertising reported in our news pages.

Coping with a cold

IN HIS article in August's MANUFACTURING CHEMIST Dr. Taylor-Robinson outlined the chequered history of common cold research and gave no hope that the production of a vaccine is a reasonably immediate prospect or is even feasible. It seems the more extraordinary that in spite of this impressive evidence from the Common Cold Research Unit oral vaccines still find a market. In the August issue of *Which?* the Consumer's Association flatly declares there is no evidence that oral vaccines give any protection against cold viruses. Indeed, as the C.A. observes, there is no such thing as a prophylactic for colds. This goes not only for vaccines but for vitamins, antiseptic gargles, nasal sprays, drops, ointments, inhalants, analgesics and decongestants. None are viricidal and the most any can do is to " help you feel better while you get better."

It is of course the lack of an effective treatment that promotes the sale of this massive armamentarium of cold " remedies." The effects of a cold can be so maddening that the victim will grasp any chance of relief—from friar's balsam to antibiotics. The advice C.A. gives its 250,000 members, advice that might well be heeded by makers of cold remedies planning their winter campaigns, is that the best relief can be obtained with aspirin and decongestants of the phenylephrine type. The Association gives the thumbs-down on vitamins, antiseptic gargles, oral vaccines and nasal sprays, drops and ointments. It is thought that the latter may prolong a cold even though they give immediate relief.

Which? lists 38 cold remedies with prices and formulæ, not that the latter will mean much to the ordinary public. Finally it urges its readers to volunteer as guinea pigs at the Common Cold Research Unit, Harvard Hospital, Salisbury.

New theory of protein synthesis

A MAJOR ADVANCE in understanding the biological mechanism underlying the ability of living cells to synthesise proteins is claimed by Dr. Carl Woese of U.S. General Electric research department.

It is known that ribonucleic acid (RNA) determines the types of proteins the cell manufactures. RNA is made from long chain combinations of four different molecules called nucleotides. The RNA molecule serves as a pattern for assembling protein molecules, which are themselves made from relatively simple long chain amino acids. About 20 different amino acids have been identified, and their order in a protein chain determines whether it is, for example, part of a red blood cell or of a muscle fibre.

It has been speculated that the order of the nucleotides in the RNA chain constitutes a code that determines this structure in the proteins produced by the cell. Working on a theory first proposed by Dr. Martynas Ycas, Dr. Woese reasoned that only a small number, or perhaps only one, of the many possible codes based on combinations of three nucleotides could be correct. He developed his code by making the combinations fit the proportions of the amino acids known to exist in certain viruses. The order of the nucleotides was arranged so that the fewest changes were required in the code to explain the differences between certain nearly identical proteins which differ from each other in only a few of their amino acids. Since such slight changes in proteins occur by mutations in the RNA, and mutations are very rare, the smallest possible change in the code is the most likely one. The code developed on these two bases was found to fit practically all the other data available on protein structure, and thus appears to be a good approximation of the true code. Before the code can be refined further, it will be necessary to obtain precise information about the structure of additional proteins.

The code has many implications for future biological research. For example, it suggests that certain types of mutations are much more likely than others because of possible ambiguities at certain points in the RNA chain. It is also likely that certain arrangements in the RNA molecule are avoided for the same reason—a very ambiguous code might make errors so frequent that the organism could not survive. The code also implies that certain specific mechanisms may be at work in the synthesis of proteins within the cell. If so, the code may give a better understanding of the exact ways in which a cell reproduces itself and carries out its other functions.

Israeli drugs—a promising start

THE pharmaceutical industry is among the oldest in Israel, the first plants having been established by German immigrants in the 30s. Today there are a dozen firms and a total production worth some 15 million dollars of which over 2 million dollars, mostly antibiotics, are exported. Most firms are formulators, but the larger ones are engaged in the organic synthesis of substances such as tranquillisers, anti-histamines and stable vitamin A from basic materials. Poliomyelitis (Salk), diphtheria and smallpox vaccines are prepared as well as veterinary sera.

A recent survey, conducted under Government auspices by a committee of scientists, concluded that the drug industry has good prospects because it can rely on readily available raw materials and scientific manpower.

Three lines of development are envisaged, namely:

(1) Fermentation processes: specific and broad-spectrum antibiotics, industrial enzymes and vitamins of microbial origin.
(2) Steroids and related materials from plant extracts.
(3) Organic synthesis of high-value drugs.

A promising start has been made on these de-

velopments because of Government encouragement of foreign investment and know-how. For example, Miles Laboratories are establishing a fermentation plant for citric acid, a French company has established a plant for extraction of alkaloids from local and imported plants (valerian, reserpine, digitalis, etc.), and an American company is establishing a plant to make steroid drugs.

Israeli pharmaceuticals have gained wide acceptance in foreign markets, both in nearby countries such as Turkey, Cyprus, Greece, Roumania and Bulgaria, and in Asian and African markets.

Israel enjoys the advantage of having a well-developed network of research institutes of international standing and ample resources of scientific manpower. Research costs in Israel tend to be lower than similar work conducted abroad and Israeli institutes have been doing contractual research on behalf of foreign companies.

CNS drug research

RESEARCH into the effects of drugs on human nerves may help to eliminate much trial and error in testing drugs on living organisms. The investigations have produced evidence that the generation and conduction of bioelectric current through the body's nerves are inseparably associated with acetylcholine. The acetylcholine receptor protein, which combines with acetylcholine and is essential for the electrical activity of the nerves, has also been isolated in solution for the first time by American scientists.

The experiments were carried out by Dr. D. Nachmansohn at Columbia University, New York, who used curare to test the theory that the acetylcholine system is present over all nerve fibres and provides the mechanism through the nerve for conduction of nerve impulses. Previously it was thought that acetylcholine was produced only at nerve endings in order to transmit impulses from nerve to nerve or from nerve to muscle.

In 1940 Dr. Nachmansohn stated that acetylcholine was not a neurohumoral transmitter but a key participant in all intracellular bioelectrical processes. The compound is vital to the generation of electricity along all conducting fibres, and the substance combines with a receptor protein to change the nerve's permeability to ion movements. The changes in permeability temporarily alter the nerve's electric potential, making possible the conduction of the impulse. An enzyme, cholinesterase, controls the duration of the acetylcholine activity by destroying the compound a few millionths of a second after it acts.

Proof of this fact was obtained by using curare to block impulses along a single nerve fibre. When curare solution was placed on the Ranvier nodes, points at which the structural barrier round the nerve is very thin, it was found that the passage of impulses down the fibre was blocked. The curare had combined with the acetylcholine receptor protein which prevented acetylcholine from causing a change in permeability to ions in the nerve, and therefore blocked the impulses. This strongly suggests that acetylcholine is produced all over the nerve.

More recently cobra venom was applied to nerve fibres of the squid. Cobra venom contains enzymes which reduce the lipid barrier round the nerve. After the treatment curare was applied to the nerve fibre and it was found that electrical activity was reversibly blocked.

The results of these tests may mean that in future, by testing the action of new drugs on an isolated acetylcholine receptor, it will be possible to synthesise more efficient CNS drugs as well as providing an understanding of many aspects of neurological diseases.

Smells that sell

MORE and more industries are using aromatic chemicals and essential oils to help their sales.

One ingenious idea is used by an American second-hand car dealer. He uses two odorising agents which are supposed to make old cars smell like new. One is applied to the car's upholstery and the other is rubbed on to the floor mats. Another product is supposed to make black tyres smell " like newly polished shoes."

Another idea comes from a laboratory in New York, which offers a rubber finger cover for bank clerks which gives a floral odour to dollar notes. The same firm also produces inks for ball point pens which do not smell of ink but of fruit.

Other substances are used to make cheap plastic goods smell like real leather, both ladies' handbags and men's wallets.

Although these are all selling gimmicks, there are several instances where scents and perfumes have been put to good use. One light-hearted report comes from a man who raises chinchillas. He kept losing costly males because the females attacked them when they were placed together. The breeder's answer was to try and change the scent of the males by dousing them in Tabu perfume, but this failed. But a second attempt with a few drops of Old Spice shaving lotion did the trick and not one male was lost after this.

A new and more serious application has been the idea of putting scent to work in industrial plant. A French chemist is reported to have discovered that people work better in a pleasant smelling atmosphere. He claims that he has been able to stimulate activity and to increase the industrial output by as much as 20% using pleasant odours. Women, it seems, react more favourably than men in these tests.

Personally we consider the idea quite fallacious. What man, when forced by his wife to work among the scent of flowers in his own garden, has the slightest inclination to pick up a spade, let alone use it?

TABLET MAKING

Basic Principles
New Developments

By John L. Livingstone,* B.Sc., F.P.S., M.Inst.Pkg.

In spite of the challenge of capsules, tablets continue to be the most popular form of drug presentation. Tableting is done in almost every pharmaceutical factory. It is advisable, therefore, to regularly take stock of tablet making practice, to re-examine basic principles and make sure that the latest developments are not being neglected. This is the approach of the author of this article which is recommended to everyone concerned with tablet making.

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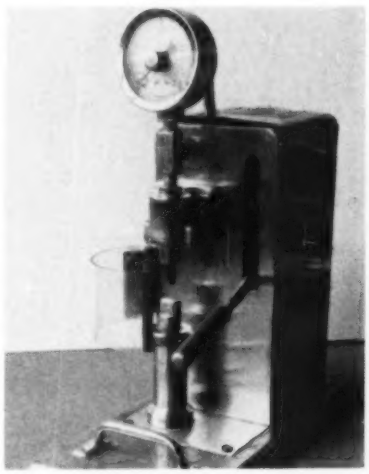
Mechanical handling has increased in extent and so has the speed of machines. Today tablets are compressed and ejected at greater speed, vibrated to remove surplus powder, moved around in bulk by mechanical equipment and packed by fast automatic machinery. This is tough on tablets. In addition they must withstand the usual hazards of transport during distribution. At the same time standards for uniformity of weight and for disintegration have become more stringent, while there are usually limits for thickness to ensure that the tablet fits the feed mechanisms of packing machines and that the correct number of tablets fill the chosen container with just the right amount of headroom.

It is proposed here not to give an exhaustive account of formulation techniques but to discuss some basic principles coupled with interesting points which arise in the light of recent practice. Many of the factors are dependent on one another, but they are mentioned separately here for convenience. New auxiliary materials are proliferating at such a rate that not all can be mentioned.

Hardness and fragility

The old tests of snapping a tablet between the fingers or dropping it on the floor from a height of about 3 ft. are still useful, but in order to ensure consistency it is usual to set a standard of hardness on a hardness tester such as the Monsanto or Strong-Cobb instruments. This ensures consistency in pressure on the machine and has some bearing on fragility. For example, a product which is intended to be chewed is compressed to a hardness of 12-14 kg. applied pressure on the Strong-Cobb scale, while one which must disintegrate in under 1 min. is compressed at only 4-6 kg. The latter needs more care in handling but can still be packed automatically. These figures apply to tablets of about $\frac{1}{2}$ in. diameter, and another tablet of this size where more normal requirements apply would be compressed to about 8 kg. Smaller tablets are judged hard enough for normal purposes at much lower readings, *e.g.* a $\frac{5}{16}$ in. diameter tablet would be quite hard enough at 4 kg.



Hardness testing indicates whether the tablet will travel and handle well. Here is the Strong-Cobb tablet hardness tester.

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Other tests have been devised.[1,2] One used in our laboratories consists of placing a number of tablets (50 or 100, depending on size) in a glass tube about 12 in. long and 2 in. diameter with rubber bungs closing both ends. The tube is rotated mechanically 100 times, so that the tablets fall from end to end each time. With each product there is a limit set to the number of chipped tablets permitted at the end of the test. An alternative method is to use a similar test but to weigh the powder produced as a result of attrition and to set a limit to this.[3]

Disintegration

Requirements vary greatly. We have the diverse examples of the quick-action antacid or analgesic, the compressed lozenge, the enteric-coated tablet and the sustained release tablet.

Disintegration rate and hardness may vary through the tablet life, generally tending to increase but sometimes to decrease. It will be influenced by the type of pack and the storage conditions. Ideally disintegration rate and hardness should remain constant. Sometimes on disintegrating an ageing tablet may break into large particles or leave a core which dissolves very slowly, in spite of the fact that the initial break-up may be rapid. Starch, particularly maize starch, is still the most commonly used disintegrating agent. The popular belief that starch aids disintegration by swelling in contact with water is of doubtful validity. In fact the action appears to be mainly a capillary penetration of water into the tablet.

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* Product Development Manager, Winthrop Laboratories, Newcastle-on-Tyne.

velopments because of Government encouragement of foreign investment and know-how. For example, Miles Laboratories are establishing a fermentation plant for citric acid, a French company has established a plant for extraction of alkaloids from local and imported plants (valerian, reserpine, digitalis, etc.), and an American company is establishing a plant to make steroid drugs.

Israeli pharmaceuticals have gained wide acceptance in foreign markets, both in nearby countries such as Turkey, Cyprus, Greece, Roumania and Bulgaria, and in Asian and African markets.

Israel enjoys the advantage of having a well-developed network of research institutes of international standing and ample resources of scientific manpower. Research costs in Israel tend to be lower than similar work conducted abroad and Israeli institutes have been doing contractual research on behalf of foreign companies.

CNS drug research

RESEARCH into the effects of drugs on human nerves may help to eliminate much trial and error in testing drugs on living organisms. The investigations have produced evidence that the generation and conduction of bioelectric current through the body's nerves are inseparably associated with acetylcholine. The acetylcholine receptor protein, which combines with acetylcholine and is essential for the electrical activity of the nerves, has also been isolated in solution for the first time by American scientists.

The experiments were carried out by Dr. D. Nachmansohn at Columbia University, New York, who used curare to test the theory that the acetylcholine system is present over all nerve fibres and provides the mechanism through the nerve for conduction of nerve impulses. Previously it was thought that acetylcholine was produced only at nerve endings in order to transmit impulses from nerve to nerve or from nerve to muscle.

In 1940 Dr. Nachmansohn stated that acetylcholine was not a neurohumoral transmitter but a key participant in all intracellular bioelectrical processes. The compound is vital to the generation of electricity along all conducting fibres, and the substance combines with a receptor protein to change the nerve's permeability to ion movements. The changes in permeability temporarily alter the nerve's electric potential, making possible the conduction of the impulse. An enzyme, cholinesterase, controls the duration of the acetylcholine activity by destroying the compound a few millionths of a second after it acts.

Proof of this fact was obtained by using curare to block impulses along a single nerve fibre. When curare solution was placed on the Ranvier nodes, points at which the structural barrier round the nerve is very thin, it was found that the passage of impulses down the fibre was blocked. The curare had combined with the acetylcholine receptor protein which prevented acetylcholine from causing a change in permeability to ions in the nerve, and therefore blocked the impulses. This strongly suggests that acetylcholine is produced all over the nerve.

More recently cobra venom was applied to nerve fibres of the squid. Cobra venom contains enzymes which reduce the lipid barrier round the nerve. After the treatment curare was applied to the nerve fibre and it was found that electrical activity was reversibly blocked.

The results of these tests may mean that in future, by testing the action of new drugs on an isolated acetylcholine receptor, it will be possible to synthesise more efficient CNS drugs as well as providing an understanding of many aspects of neurological diseases.

Smells that sell

MORE and more industries are using aromatic chemicals and essential oils to help their sales.

One ingenious idea is used by an American second-hand car dealer. He uses two odorising agents which are supposed to make old cars smell like new. One is applied to the car's upholstery and the other is rubbed on to the floor mats. Another product is supposed to make black tyres smell " like newly polished shoes."

Another idea comes from a laboratory in New York, which offers a rubber finger cover for bank clerks which gives a floral odour to dollar notes. The same firm also produces inks for ball point pens which do not smell of ink but of fruit.

Other substances are used to make cheap plastic goods smell like real leather, both ladies' handbags and men's wallets.

Although these are all selling gimmicks, there are several instances where scents and perfumes have been put to good use. One light-hearted report comes from a man who raises chinchillas. He kept losing costly males because the females attacked them when they were placed together. The breeder's answer was to try and change the scent of the males by dousing them in Tabu perfume, but this failed. But a second attempt with a few drops of Old Spice shaving lotion did the trick and not one male was lost after this.

A new and more serious application has been the idea of putting scent to work in industrial plant. A French chemist is reported to have discovered that people work better in a pleasant smelling atmosphere. He claims that he has been able to stimulate activity and to increase the industrial output by as much as 20% using pleasant odours. Women, it seems, react more favourably than men in these tests.

Personally we consider the idea quite fallacious. What man, when forced by his wife to work among the scent of flowers in his own garden, has the slightest inclination to pick up a spade, let alone use it?

TABLET MAKING

Basic Principles
New Developments

By John L. Livingstone,* B.Sc., F.P.S., M.Inst.Pkg.

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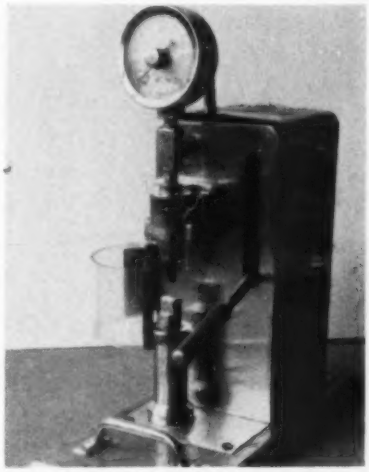

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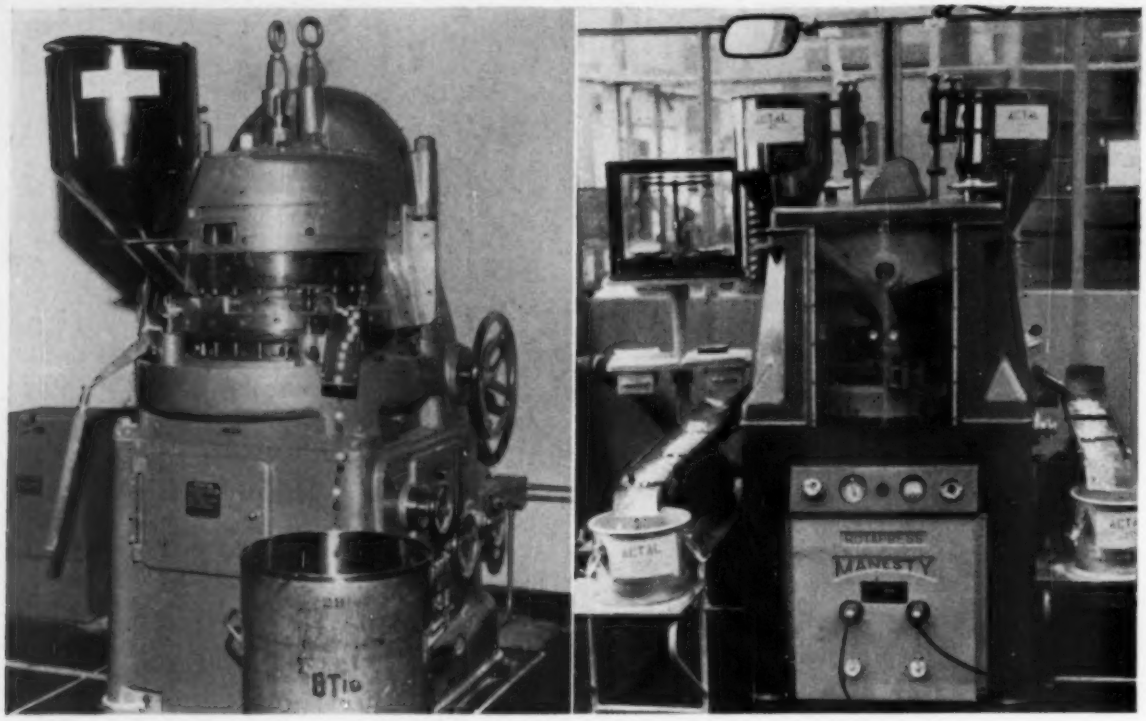


Left: Heavy duty rotary machine used for slugging made by Manesty. Right: Manesty high-speed Rotapress produces tablets at up to 4,000 per min. and has a special feed mechanism to force granules into the dies.

cient. It is wise to ensure that a constant brand of starch is used. An unaccountable difficulty in compressing one tablet was traced to a change in the brand of maize starch, although other tablets ran quite well on any brand. It is doubtful if special drying of the starch is of use except where there are very unusual stability problems, and the addition of dry starch to granules just before compression has only a marginal advantage over putting it in earlier during a wet granulation procedure. This method, however, enables better use to be made of the lubricating qualities of starch and there are therefore occasions when it is desirable. It is wise to keep a watch on the moisture content of the starch being used. If this is excessive it means that less liquid will be needed to produce granulation consistency and therefore the amount of granulating agent added may be less than usual. This is likely to cause inconsistent results during batch manufacture.

Alginic acid is a useful aid to disintegration;[4] it is rather expensive if used at its optimum level of 7-10%, but 1% gives a useful boost in many cases and can be added to about 10% of starch. It works a little better when added during wet granulation in contrast to being added dry at the end. It is of some use in keeping down dustiness on the tablet surface.[5] *Veegum*, a type of magnesium aluminium silicate, is a recent addition to the disintegrant field.[6]

Granulation

The simplest granulating agent to use is water, and moistening alone may be sufficient to form a granule where the other raw materials have some adherent properties. When using water-soluble cellulose ethers, water alone as the vehicle often causes too much swelling and stickiness, and water/ethanol or water/isopropanol mixtures may give better results. Starch paste is a safe, inexpensive and reliable granulating agent. It should be properly made and used within a few hours. It is a good idea to use a standard strength throughout the department, say 10%. Sometimes a slightly higher strength makes a significant difference, but this is not common. Addition of a wetting agent may help in cases of rather hydrophobic powders, for example sodium lauryl sulphate at about 0·125% of the final tablet weight may be used. It is sometimes desirable, especially where the active ingredient may vary from batch to batch in absorbent properties, to use a fixed amount of starch paste, but with a little less fluid than is needed to complete the granulation, and then to conclude with plain water. This allows the operator some latitude, yet the final composition of the tablet will not vary. Tablet making still depends to a large extent on the experience of the operator and this applies to granule manufacture as well as at the compression stage.

Gelatine is a very good binding agent and is best employed as an addition to starch paste. Material with a bloom value of about 230 is very suitable and it should be soaked in cold water for several hours, preferably overnight, before dissolving. This ensures maximum gel strength. It should be added to the starch paste after the latter has been made and not boiled up with the starch. Cases of mould growth on tablets containing gelatine have been seen in some climates and it has therefore been employed with caution in export production. There are now

available spore-free and long keeping gelatines which are being tried for this purpose. (It should be remembered that other ingredients, such as starch, may carry a high count of mould spores.)

Gum acacia is a traditional binding agent, perhaps the strongest commonly used. It used to be extensively used, but caution is required if present-day standards are to be met on disintegration. Many tablets tend to harden markedly in storage if made with acacia, particularly if storage temperatures are high. Other gums, such as karaya, guar and carob, have been used.

The cellulose derivatives, sodium carboxymethyl cellulose and methyl cellulose, and also sodium alginate and irish moss extract, are worth keeping available, as they may be valuable where compatibility or physical difficulties rule out other materials. Where water must be avoided and alcohol gives insufficient binding power, an alcoholic solution of ethyl cellulose—about 2-5% of 50 cps grade—may be effective. Liquid glucose (corn syrup) and simple syrup are valuable where a soluble granulating agent is needed. If a good proportion of sugar is present in the tablet, wetting with water is sufficient for granulation. Care with this method is necessary, as a tendency to ball-up in the mixer is sometimes seen where the sugar content is high, and tablets may tend to be spotty if the sugar is made too wet. Mixing should not be prolonged.

The formulator will be faced with the experience of deciding the proportion of granulating solution to be used during work on, say, a 2-5 kg. scale, only to find that, when scaled up, this proves to be too much for the larger batch. Some materials are prone to produce spotty tablets if slightly over-wetted and the best way to decide the amount to use is to add just enough to cause the mix to form a ball in the hand, but not enough to cause it to stick to the sides of the mixing vessel. If the batch size or type of equipment is changed, it may be necessary to change the amount of solution. A mass intended to go through a comminuting machine may need to be wetter than one going through an oscillating granulator, while some designs of mixing equipment are more efficient with doughy materials than others and achieve a suitable consistency with less added fluid.

Slugging

Precompression or slugging is more common in the U.S.A. than in this country. There are some cases where it is obligatory, and wherever possible a heavy slugging machine should be employed as this gives better results and avoids the great strain and wear that slugging can exert on a conventional machine. With abrasive materials such as aluminium hydroxide, sieving of the powders through a 40 mesh sieve is a wise precaution before feeding to the machine, as larger particles getting between punch and die wall may cause damage. It is normal to add some of the lubricant at the slugging stage and some before final compression, and the optimum proportion has to be ascertained in each case.

Slugging is usually used where materials are moisture-sensitive, but should not be forgotten as a method for use with a volatile, or low melting point, raw material. In the case of a moisture-sensitive drug which will not slug, non-aqueous solvents may be tried for granulation, but anything other than alcohol may raise problems on account of toxicity hazards to operators or flammability risks. It should be mentioned that even if a good granule cannot be obtained, a coarse or medium powder, down to about 40 mesh, may compress satisfactorily, given certain precautions discussed later.

Newer types of granulating equipment are now being made available and some will provide certain advantages over existing methods. Among these are the Alexanderwerke machine which forces the moistened mass between rotating rollers and extrudes it through holes into the hollow centre of the roller, whence it is discharged through an open end. Another type is the Chilsonator, which resembles in outline the rollers used for pill cutting, but with horizontal corrugations. On a different principle is the Wurster apparatus where the powders are air floated in a chamber and the granulating solution sprayed in. There are soon likely to be other machines which will enable less solution, or even none at all, to be used.[7]

Excipients

Starch, lactose and calcium phosphate are probably still the most commonly used and most useful excipients. In some factories a standard excipient granule made of lactose with starch, or lactose with calcium phosphate is kept as a stock item. Over 20% of starch may make the tablet too friable, and lactose makes a granule which on occasions may be too brittle although it disintegrates readily. Sucrose finds a place occasionally, especially in compressed lozenges. Objections to the use of sugar on the grounds that the tablets may be contra-indicated for diabetics are usually not valid, as the sugar content is so small as not to matter. Mannitol has recently become popular as it gives the tablets a pleasant smoothness in the mouth and is a good excipient. It is useful for sublingual tablets or those which have to be chewed or dissolved in the mouth.

Lubricants

By far the commonest lubricants used are talc, stearic acid and magnesium stearate. The main points to be considered in using these may be summarised thus:

(*a*) *Talc*—gives the granules good flow properties in the hopper and feed-frame or shoe. It is the least efficient of the three as a die lubricant,[8] but has few other objections. About 4-5% is usually needed.

(*b*) *Stearic acid.* This is quite efficient but beware of incompatibilities. About 2% is needed. Because of its low melting point it may cause trouble with tablets during heat-sealing in aluminium foil and foil laminates, producing a spotty surface.

(*c*) *Magnesium Stearate* is the most efficient die lubricant of the three—about 1% is usually required. It tends to slow down disintegration because of its water-repellent properties and may also have incompatibilities, *e.g.* with aspirin. It is excellent for giving a smooth surface and clean lettering.

It will often be found that a combination of these three is needed. Thus magnesium stearate may be desirable in a lettered tablet, but because of disintegration difficulties must be kept down to say 0·125 or 0·25% and the remainder of the lubricant made up with talc or stearic acid. If weight variation occurs it is probably due to poor granule feed and talc may put this right. Waxes, liquid paraffin, etc., are rarely of great value, but there are cases where either these or a hard oil such as hydrogenated castor oil, applied in a solvent, may be usefully employed. An oil with a

melting point of about 80°C. should be used. It should be remembered that dry starch itself has some lubricant properties both in the die and the hopper. Lubricants for soluble tablets may present a difficulty. Boric acid is generally contra-indicated on toxicity grounds. The higher molecular weight polyethylene glycols may sometimes help.[8]

Sperandio and DeKay's suggestion of sodium acetate and sodium benzoate[9] is useful and worth following, but the physical state of the acetate influences the result—some suppliers' materials being better than others. There seems to be no advantage in adding lubricant at the wet granulation stage and more is then usually required. The amount of lubricant needed will vary somewhat according to whether a single punch or rotary machine is used, whether tool steel or tungsten carbide lined dies are used and whether the die clearance is large or small. For example, in American practice a greater die clearance and less lubricant are usually used. Many simple crystalline substances will compress without added lubricant.

During slugging operations particle size of the powder fed to the press may be important, a finer powder often runs much more easily with the same amount of lubricant. This is contrary to expectations as the surface area is then greater. Signs of insufficient die lubricant are: vertical score marks on the edge of the tablet, delayed dropping of the bottom punch assembly in single punch machines, and in more extreme cases the squeaking or grinding sound of the machine is indicative. Usually less lubricant is needed for a rotary machine than a single punch one, but the speed of the machine will also make a difference.

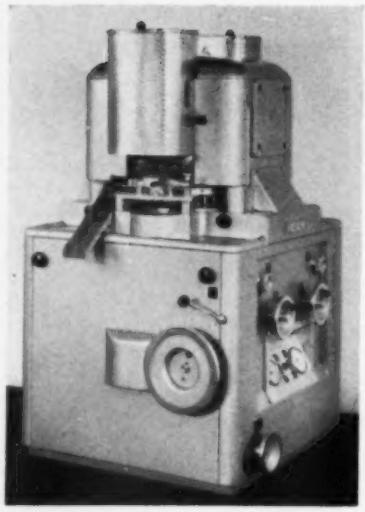
Colours and flavours

An even spread of colour in a tablet is often difficult to achieve.

Methods recommended are:

(*a*) Use of starch which has already been coloured with a dye solution, dried and powdered—useful for a slugged tablet.

(*b*) Incorporating the dye in the starch paste. A difficulty sometimes encountered during wet granulation is that, during drying, patches of more intense colour form at the granule surface. This can sometimes be prevented by exposing the granule to room temperature for a while until preliminary drying occurs, then completing in an oven at fairly low temperature. In one case observed, an acid and an alkaline ingredient were both present in a tablet and took up the added colour, each to give a different hue.



Kilian's new type NRD tableting machine which has a potential output, by the use of multiple punch tips, of 850,000 tablets per hr. No forced feed is necessary and there is a pre-pressure device for eliminating excess air in the material. All adjustments are calibrated. There is centralised automatic lubrication and all controls are grouped at the front of the machine. Cleaning and maintenance has been reduced to a minimum.

Flavours call for little comment. The flavour manufacturers supply dry flavours where the flavouring is incorporated in a protective base, *e.g.* by spray drying from a gum solution. It is usually necessary to use from 1 to 5% of these. Essential oils may also be introduced into the tablet, but care should be taken in incorporating them as they may take up the lubricant.

It is sometimes necessary to provide a placebo tablet for clinical trials and a bitter taste is required. Quinine may be used as it is bitter enough at well below active levels. The vegetable bitters, such as quassia, are not usually strong enough for this purpose. A new bitter compound, *Bitrex*, is an improvement on these. Fading of flavour may be influenced by the tablet base—alkalinity often accelerating this. A coating of ethyl cellulose or zein may be worth while as a sealing device,[10,11] but good packaging is important. This is particularly so in that some alkaline tablets also pick up foreign odours easily, *e.g.* from perfume or tobacco in a user's pocket or handbag.

Some special formulation problems

(**a**) **Effervescent tablets.** Generally low humidity conditions are required during manufacture and packing, but in some cases satisfactory results may be achieved with a relative humidity of 40-50% at 65°-70°F. Aspirin requires a much lower R.H. level—20% or less. The usual technique is to make the two parts of the granule separately and mix dry immediately before compression. Sometimes, however, the old type of partially fused granule base is used. It is an advantage, if wet granulation can be avoided altogether. If this is not possible, alcohol or liquid glucose with the minimum amount of added water should be tried. The granulating and lubricating agents frequently must be completely soluble. As rapid disintegration is the aim a relatively large amount of effervescent base is usually used and the tablet has a large surface area, being made thin and of large diameter. It should not be compressed too hard. These conditions make a fragile tablet and packing and handling must be carried out carefully.

A disintegration time of not more than 2 min. in water at 70°F. is usually required.

(**b**) **Layered tablets.** These usually consist of two layers, occasionally three. The method is normally adopted to separate two incompatible ingredients, and although some reaction will occur at the junction, it is in practice negligible compared with that occurring in a mixture of ingredients. The layers may be of different colours and frequently this is done to enhance the appearance. The two main problems are to get the two layers to adhere together and to prevent traces of one layer getting into the other. One layer is compressed first and the second granule filled on the top, and the whole then compressed. The first compression must be as light as possible, consistent with forming a clean junction at the interface—too much compression at this stage giving a poor joint. Various scavenging devices—

(*Continued on page* 461)

Piping Up Chemical Plants

By W. H. Homer*

Pipework accounts for probably 15/30% of the cost of a chemical plant, but it is not always planned, designed and installed as efficiently and economically as it could be. A great deal could usefully be written about this neglected but vital subject. In this short article the author, a practical piping engineer, discusses the steps in piping up a medium-sized organic chemicals plant.

ON the threshold of space, with speeds already achieved which were undreamed of even a decade ago, man's increasing quest for faster, bigger, better means of travel, communication and production, has brought complex problems as more becomes known of the materials which are being used and will be used in the future to further our technical progress.

No better example can be found than in the chemical industry, where the simple tube or pipe employed centuries ago by the Romans for conveying water has been translated into a vast network of engineering detail, constructed from a host of different materials to meet the extremes of operating conditions imposed by pressure, temperature and corrosion.

Volumes could be written on this extensive and rather neglected subject—extensive because each year brings new processes frequently demanding extensions in either type, size or duty of pipework—neglected because despite sometimes bitter experience, by the very nature of plant construction detailed attention can only be paid to pipework in the later stages of design, when the kitty is sometimes running low.

With no hope of covering the entire field in a short article, let us postulate a medium-sized company, employing 2/300 people, operating an organic plant producing dyestuffs, solvents, etc., and about to build a new plant or extension. We will examine the factors common to all pipework systems of this type but, even limiting our survey to this extent, an enormous variety of processes *could* be involved, and as so many decisions affecting pipework depend entirely on the *particular* process in mind, our conclusions are bound to be rather generalised.

The plant will comprise a number of small units producing small quantities of a wide variety of products. The operating company will want to make frequent changes to keep abreast of new techniques and basic information of this sort is important in considering pipework. If a process is to be frequently modified, flanged rather than welded joints should be used, always supposing flanges meet other design factors.

The process will have been established by the chemist, considered by the Board and referred to Sales Research for a report on market potential. Development Department will have prepared an estimate of the cost of building a plant to produce the quantity for which a market exists and will set the selling price. The engineer is finally instructed to build a plant to produce *x* tons within a given budget figure.

It is worth reflecting on the above chain of events and to consider that whilst so far little attention has been given to pipework, changes in plans could drastically alter the installation, hence the need to ensure a high degree of flexibility in whatever means are eventually adopted to complete pipework. Assuming that all services are available, it is customary to consider the project under these headings:

1. Civil works.
2. Plant items—vessels, heat exchangers, pumps, separators, etc.
3. Electrical.
4. Instrumentation.
5. Pipework.

At this point the company must decide how they are going to build the plant—

a. By engaging consultants.
b. By appointing a main contractor to design, procure and erect the entire plant.
c. By undertaking the design and supervision themselves and engaging specialist contractors.

Clearly the relative size of the project and of the company are going to influence this decision. Let us assume they elect to build themselves.

Setting aside any detailed reference to civil or electrical work, attention will first be directed to main plant items which have to be purchased. The company may wish to design vessels and perhaps heat exchangers themselves, making the first call on the drawing office.

Flow sheet

Having decided on the number, type, size and location of vessels, etc., a mechanical flow sheet is prepared from which a single-line piping layout or arrangement is produced. At this stage the engineer must decide whether he is going to fabricate and erect pipework with his own staff or engage a specialist pipework contractor. It is generally preferable, and usually the practice, to sub-contract this work. If he is to use his own men they will be drawn from the maintenance staff. Either routine maintenance is going to suffer or, if there is sufficient labour available for both duties, then an unnecessarily high labour force is being maintained, unless a proportion is *permanently* employed on new construction. Few companies build fast enough to satisfy the latter condition. Furthermore, it is highly probable that some of the pipework will be coils, jacketed tubes, rubber-lined pipework or other assemblies which require to be shop fabricated—a portion of which will in any case have to be bought outside. If so, detailed drawings of such items will have to be prepared for the use of the supplier, throwing a further load on the drawing office and leading to the difficulties which arise when men from one company are engaged in the erection of pipework fabricated by another.

Better results will generally be obtained by engaging a competent contractor with experience of this type of plant, preferably with shop fabricating facilities sufficient to manufacture any prefabricated

* William H. Capper and Co. Ltd.

sections required. By so doing the engineer frees himself from a mass of detail which then becomes the sole responsibility of the contractor. From the general arrangement drawing, the contractor will have to produce whatever detailed drawings are necessary for his own use at site, or for the manufacture of shop fabricated items. Any delay in delivery to site of the latter is again the direct concern of the contractor, as is also the quality and dimensional accuracy of the various parts.

Later in the article reference is made to the form of tender and selection of contractor. To revert to the general pipework layout, this will of course include details of pipeline sizes and at this early stage serious thought should be devoted to the question of supports. This should present little difficulty in new construction areas, but supporting arrangements *are* frequently overlooked until the last minute and there are all too many instances where completion has been either severely disrupted or even delayed for want of attention at a much earlier stage.

Materials of construction

Materials of construction could well form the subject of a book. While it is necessary for the contractor to have experience of all the various materials to be used on a wide variety of pipework contracts, so that his experience is likely to exceed by far that of the average maintenance staff, the actual selection of materials should be made by the company as they are obviously more familiar with the chemical properties of their own products than any contractor.

From a wide range of materials which *can* be employed the following are commonly used:

Mild steel. Offers the widest choice in jointing arrangements, virtually unlimited as regards pressures, and still the cheapest to buy. But its use is strictly limited by its vulnerability to corrosion. Various forms of lining, notably rubber, provide adequate protection against some types of corrosive attack where the strength of steel is an advantage. Extensive runs of lined pipes and fittings are best shop fabricated.

Stainless steel. Very widely used in both F.M.B. and F.D.P. quality to resist corrosion, discolouration and for cleanliness. It is three times the price of mild steel, but it is available in lighter wall thicknesses and has high scrap value.

Plastic. Many reliable qualities are now available in sizes ranging from ¾ in. to 18 in. Injection moulded fittings up to 6 in. size are freely available. Screwed, flanged or solvent welded joints are quite suitable for the low pressures usually encountered. Plastics can be used for relatively high pressures when reinforced by bonded glass fibre. Use is limited by temperature considerations and care should be exercised in the use of some qualities at temperatures exceeding 100/150°F. It has high resistance to corrosion, is light and easy to handle, and the smooth bore gives good flow characteristics. Low thermal conductivity. Cheaper than stainless steel and particularly well suited for underground service where the usual need for small intervals between supports is obviated.

Pipework in copper, aluminium, glass, *Keebush* and *Hastelloy* is specified less frequently. Each material possesses resistance to corrosion, abrasion or heat resistance and this makes them suitable for special applications. But relatively high cost and some difficulties in fabrication make them less popular than the first named.

Installation work presents no particular engineering difficulties and is best examined in the light of other design considerations which govern how the work proceeds. Again factors affecting one type of material do not necessarily apply to all, but there is a certain amount of common ground.

Welding

The usual considerations apply regarding selection, supervision and test of operatives. Any tendency towards a casual approach to this most important operation must be rigorously suppressed. While the need to preheat, stress relieve or X-ray rarely arises on account of the gauge of material employed, strict control must always be maintained by the procedure laid down for issue of rods, storing of materials, maintenance of equipment and tools and frequent examination of prepared surfaces.

It is sound and common practice to weld small bore mild steel lines by the oxy-acetylene process. Sizes 2 in. and above will ordinarily be electrically welded.

Stainless steel welds will be made by the metallic arc or argon arc process, depending on the wall thickness of the tubes. Argon welds are preferable on the lighter gauge tubes and where the product is particularly corrosive, it is sometimes necessary to have an argon purge internally during completion of the root run.

Joints

A balance has to be struck between the conflicting demands of security and ease of maintenance or modification, with the former taking preference. A completely welded line will not leak but it is difficult to inspect and clean. Every flanged joint is a potential leak, but where certain linings are specified (rubber, lead, glass, *Lithcote*, etc.) the extensive use of flanges cannot be avoided and simplify the problem of maintenance.

The solution is usually a compromise, remembering that joints are expensive and should be included only where absolutely necessary to facilitate erection and maintenance.

It is usual to butt weld adjacent lengths, providing flanged joints at 60 ft. intervals.

Bends

To reduce friction losses and interference or resistance to flow, changes in direction should be kept to the minimum and, theoretically, sharp bends avoided.

However, the need to limit the size of large plants, particularly in petrochemicals where very large pipes are used, has led to the development of a complete range of forged steel fittings in both mild and stainless steel quality, which offer a radius 1½ times the bore size. These fittings, supplied in a wide variety of wall thicknesses, are of uniform thickness throughout, available from stock, and are now so commonly employed in all manner of pipework installations that their use on small chemical plants has become generally accepted. Furthermore, their smooth bore and uniform cross-section offset to some extent the higher friction loss resulting from their smaller radii.

If flow characteristics are of paramount importance larger radii bends must be employed either welded in, offered as flanged fittings, or formed in long lengths of tube.

Expansion

Provision for expansion presents few difficulties on plants where only

moderate temperature variations are expected. The small amount of movement can usually be absorbed at bends if anchor points are carefully chosen.

If long straight runs necessitate special provision, this can be provided in the form of horseshoe type loops, sliding joints incorporating some form of gland or stainless steel bellows. Available space, cost, product and materials in use will determine which is the most suitable. Loops certainly occupy more space, require more elaborate supports and are probably less convenient than bellows. Some types of plastic pipes may expand up to five times the equivalent of mild steel, and whilst their use is limited by temperature, this point should be heeded.

Valves

Their type and use will be dictated almost entirely by process design. Gate valves offer the minimum friction losses and when fitted into lines with flanged joints provide useful breaks for convenience of erection, maintenance and test. Take care that they are sited for ease of operation.

Supports

Little information is given on general arrangement drawings, but it is probable that supports will represent about 25% of the cost of pipework installation and are therefore worth close attention.

Full use should be made of existing structures, but these can be and often are overloaded and if this is likely to be the case alternative arrangements should be made at an early stage before final location of vessels, etc., makes it virtually impossible to provide adequate support without altering the general run of the lines.

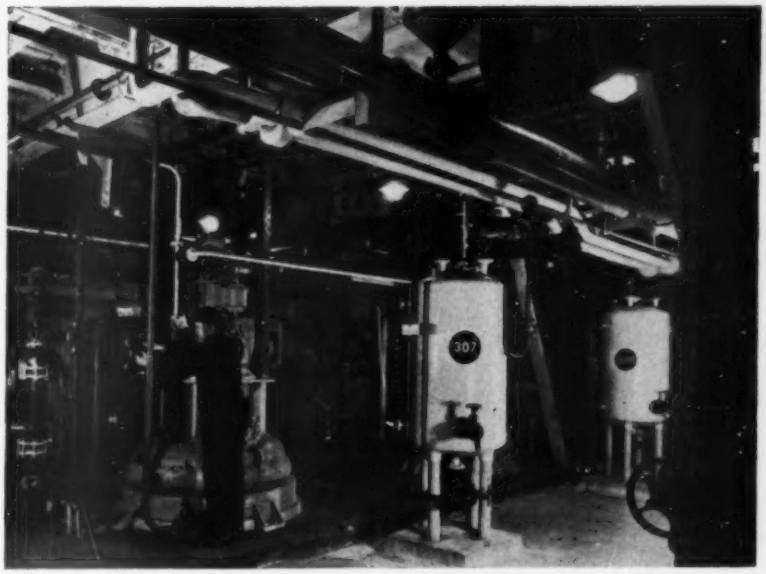
For cold service, rigid U-bolt type supports are bolted either direct to steelwork or to brackets welded thereto.

For heated lines free moving supports are used in the form of drop rod and band clip, the pipes being suitably anchored between expansion points.

Lagging and electrical insulation

This may form part of the pipework contract, but it would be subcontracted to specialists in most cases.

In the production of certain classes of non-polar solvents there is a possibility of a build-up of static electricity to the point where a spark may be created. Provision must be allowed for the earthing of the pipework system in such cases. Readings should be taken at various points and a suitable bond to earth provided where resistance exceeds a given level.



GOOD PIPEWORK. Part of the new fluids plant at Midland Silicones Ltd., which exemplifies well-ordered pipework layout. Mains are nested close to supporting structures with minimum obstruction to plant operation and valves are easily accessible.

Inspection and test

Details of the exact procedure required should be included in the tender documents, together with a clause governing the guarantee period. The installation is usually subjected to either hydraulic or air and water test, selecting convenient lengths between valves or flanged connections. Thereafter, the contractor is generally responsible for a period of 12 months, fair wear and tear accepted.

Getting tenders

The successful use of a specialist pipework contractor depends on the manner in which he is engaged. Therefore the form of tender is important.

If the pipework layout drawings are available in sufficient time to allow for tender, purchase of materials, fabrication, erection and test to meet completion date, the engineer can call for a lump sum contract price which is the most suitable basis, when majority of attendant factors can be made known to the tenderers.

If design is not so well advanced or insufficient time is available, three alternatives remain:

(1) Tender on estimated tonnage. This is accepted practice for refinery work because of the repetitive nature of the work and the vast quantities involved, but it is quite unsuited to small contracts.

(2) Invite quotations on a bill of quantities. Where a flow sheet is complete but the piping layout is not available, an estimate is made of quantities and prices called for based on a confirmed schedule of rates. All work is measured on completion. This method provides some guide to total cost, depending on accuracy of material estimate and a measure of control, assuming that revisions to layout are likely.

(3) Erect on daywork basis. This is only employed where little or no information is available for the preparation of either drawings or bill of quantities, and plant has to be on stream by target date to meet market demand.

There are obvious weaknesses and results depend almost entirely on knowledge and ex-

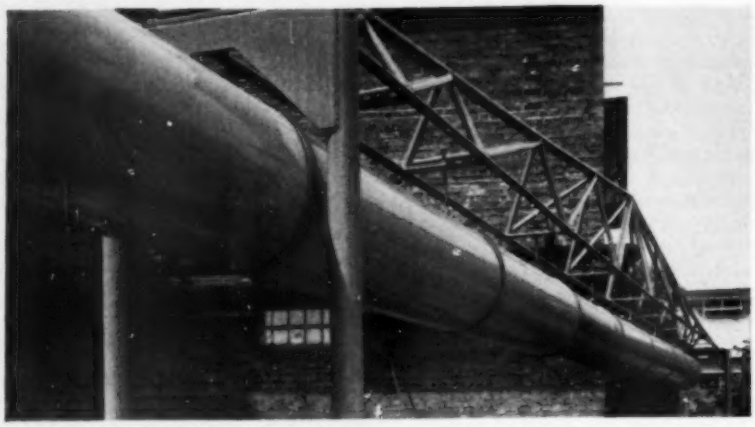
(Continued on page 452)

PIPES FOR CHEMICAL DUTIES

PLASTIC PIPE FOR CHEMICAL PLANTS

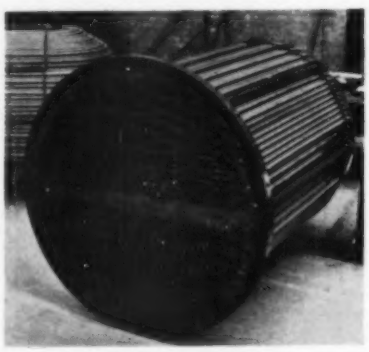
THE chemical industry, while superficially the most likely user of plastic pipe, has in fact lagged behind other industries in the tremendous upward surge of plastic pipe consumption of the past three years. The reason for this is not far to seek. While the chemical resistance of thermoplastics is equalled probably only by glass, the upper temperature limit of around 140°F. makes the material unsuitable for many applications. However, many miles of pipework operate at temperatures well below that of the domestic hot-water system and plastics like polyethylene, polypropylene and PVC are finding increasing scope. The strongest and most easily handled of these plastics is unplasticised PVC. Already far cheaper than copper and with a chemical resistance superior to stainless steel, it has long been available with a wide range of fittings. Pipe from ½ in. up to 18 in. in diameter is now extended in a new improved compound PVC known as *Hika 80*. This is the first PVC tube to offer significantly improved impact strength without detriment to either its longevity, strength or corrosion resistance. Dropped weight impact tests show that a 2 in. tube of 0·215 in. wall thickness will withstand an impact load of 180 ft. lb. at 70°F. through the medium of a ½ in. radius striking nose.

Ease of handling, the efficiency of the solvent welded joints and its clinical cleanliness all contribute to the increasing appearance of PVC in effluent lines, acid and alkali pipework and demineralised water lines. Another range of plastic pipelines is the " Polyorc BH " series of high impact PVC tubes and fittings. Compared with other types of PVC it is claimed to have extremely high impact strength. It does not contaminate the products conveyed and has a particularly smooth bore, giving a high rate of flow with minimum build-up. Comprehensive ranges of tubes and moulded fittings are available for both plain cemented and screwed joints and moulded socket stub flanges can also be supplied for cementing to tube ends and the joints completed with malleable iron backing plates and rubber gaskets.



High impact Geon PVC pipe, 15 in. dia., carrying chemical effluent at a High Wycombe factory.

Polyorc BH can be easily drilled, sawn, or machined or formed and bent after heat-softening. Welding and fabrication of special items can be undertaken using a hot air gun and " BH " filler rod. Special cleaning fluid and solvent cement are provided for cemented joints. The pipelines may be used at temperatures up to about 50°C. although with rising temperatures the tensile strength is reduced. In certain circumstances this temperature can be exceeded when low pressures are involved, but the advice of the makers should be sought when special applications are being considered.



INTRICATE PIPEWORK

In this heat exchanger, which is 7 ft. 7 in. long × 5 ft. 2 in. shell diameter, no less than 8,000 ft. of tubes have been nested to give 2,000 super feet of heating surface. 560 stainless steel (FDP-Ti stabilised) tubes were cut and bent to form hairpins of 20 different lengths. This intricate piece of pipework was made by Wm. H. Capper and Co. Ltd. for the Distillers Co. Ltd., to heat highly corrosive chemical liquid with waste steam. The tubes are subjected to a pressure of 45 p.s.i. at 275°F. under normal working conditions. Two units of this kind have been delivered to the Treforest works of the chemical division of Distillers for use in the manufacture of CO_2.

PVC PIPE FOR EFFLUENT DISPOSAL

Recently T. B. Ford Ltd., manufacturers of blotting paper and filtration media, decided to modernise their effluent disposal system. Previously effluent had been carried from the factory in a series of wooden troughs. The company now wanted a material that had a better appearance, was easy to install, and could be used out-of-doors without the need of continual maintenance. They chose pipe in Geon high-impact PVC.

At one stage, the system passes over a stretch of water several yards broad, and it was essential to use a material that could cross this gap without the support of elaborate bridging. In this respect PVC pipe offered considerable advantages over competitive materials due to its combination of strength and light weight. Furthermore, maintenance costs have been cut because the Geon pipe is weather resistant and the need for regular repainting is entirely eliminated.

The pipe carries waste produced in the manufacture of blotting paper and filtration media, and this waste contains dilute chemicals. More-

over, those parts of the system which are indoors function in an extremely damp atmosphere. Here the corrosion resistant properties of Geon PVC proved invaluable. It was also found to have a price advantage over stainless steel or rubber-lined pipe, the possible alternatives.

In all, some 800 ft. of 15 in. dia. pipe have been installed. T.B. Ford report that they are very satisfied with the installation and plan to use PVC pipe in other parts of their plant.

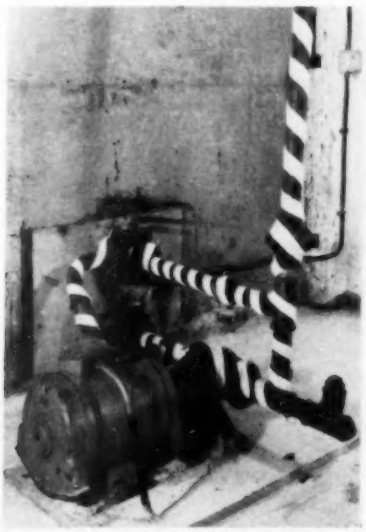
GLASSED STEEL PIPELINES

Glassed steel pipes and pipe fittings to suit most chemical industry needs are supplied by Enamelled Metal Products Corp. (1933) Ltd. These Pfaudler pipes are available with fixed or loose flanges to British Standard Table or ASA drillings. They carry a one year guarantee and are fully electrically tested against the most severe chemical conditions.

The physical and mechanical bond between the glass and steel assures a material of construction with a strength surprising to those who associate the word "fragile" with glass. The strength of the glass to metal bond in glassed steel has been demonstrated in several tests, one of which proved the inability of a dead weight load of 11,000 lb. to separate two 4 in. diameter steel discs which were glassed and fired face to face. In other tests glassed steel plates have been twisted to the elastic limit of steel, yet the glass to steel bond and the glass itself remained intact.

Glassed steel is not however indestructible. Hit it hard enough with a hammer and it will chip, but any damage of this type is limited in extent by the unique character of glass fused to steel. Furthermore, because of the interlocking chemical action at fusion temperature fractures will not run as will be found with normal pane glass.

With sensible care glassed steel can be relied upon for years of dependable service and not surprisingly has widespread application in the process industries.



Heating tapes on 2 in. pipes maintained at 150 C.

HEATING TAPES FOR PIPELINES

To keep pipelines hot electric heating tapes are being used to an increasing extent. *Isotapes* made by Isopad Ltd. are made in a large number of standard sizes between 1½ ft. to 200 ft. lengths and in a great variety of loadings per foot to cater for all heating duties from frost protection to high temperature work. Simple graphs and tables in Isopad's catalogues show the required wattage loading for various pipe bores and temperatures for which a suitable heating tape can then be easily chosen. Special flameproof designs are available and, for example, are used at Port Talbot Chemical Co., Ltd. for benzole lines.

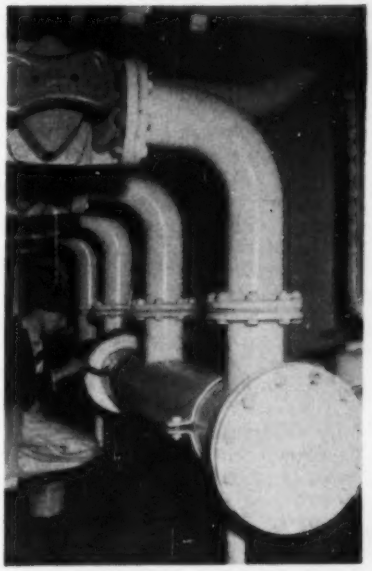
A full range of thermostatic controls is available.

As good thermal insulation is used over the tapes and pipes; this has been found a most economical and efficient method to solve pipe heating problems.

AUTOMATIC TUBE BENDER

Suitable for mass production of tubular products and any repetition pipe bending operation, a new automatic production tube bending machine, capable of producing 500-600 bends per hour, has been marketed by Chamberlain Industries Ltd. The machine, designated the *Staffa-Herber* SBA 28, has a maximum capacity for steel tubes of 1½ in. o.d. ×16 s.w.g. thick and non-ferrous tubes of larger sizes.

Among the many new features of this machine is a patented device which permits right- and left-hand bends to be made without resetting the machine and tooling. This is possible even when successive bends are directly adjacent to each other, that is, without intervening straights,



Acid feed lines in a large chemical factory in which all pipework and gaskets are lined with ebonite.

and the device also allows in certain cases for bends of different radii to be produced without the necessity of changing centre formers.

A pre-selector on the control panel permits up to 12 bending variations without resetting any levers and is automatically controlled after each completed bending operation. The bending head returns automatically and the workpiece is ejected from the centre former groove.

RUBBER-LINED PIPEWORK

Dunlop offer a pipe lining service to the chemical industry. Rubber and ebonite linings are applied for protection of metal pipework against internal corrosion and/or abrasion.

For abrasive purposes soft rubber linings are applied, and in one particular application where silica sand is being blown through 6 in. bore pipework soft rubber linings have increased the life of the metal pipe to six times normal.

Considerable quantities of corrosive liquor are carried in metal pipes, and rubber lined metal pipework combines the strength of the steel with the corrosion resistance of the rubber.

A wide range of rubbers is available which will accommodate most alkalies and a large number of acids with the exception of the concentrated oxidising acids such as nitric, chromic, etc. Where traces of oil

or organic solvents are present in the liquors, synthetic rubber linings can be applied.

Five years ago, Dunlop produced a special heat-resisting ebonite lining for use at temperatures in the region of 100°C., and now claim that this particular compound, *Duraline*, will resist these higher operating temperatures without the tendency to harden, which has hitherto resulted in embrittlement of ebonites and premature cracking.

A pipeline lined with this material has been in operation for over two years carrying dilute sulphuric and hydrochloric acid at a temperature of 95°C. without failure.

In addition to the lining of customer's own metal pipework, the metal pipe itself can be purchased by us to customer's requirements.

In all cases the metal fabrication must meet certain requirements to ensure a first-class rubber lining job, and details of these requirements are given in a leaflet which can be obtained on application from Dunlop's Chemical Plant Lining Group.

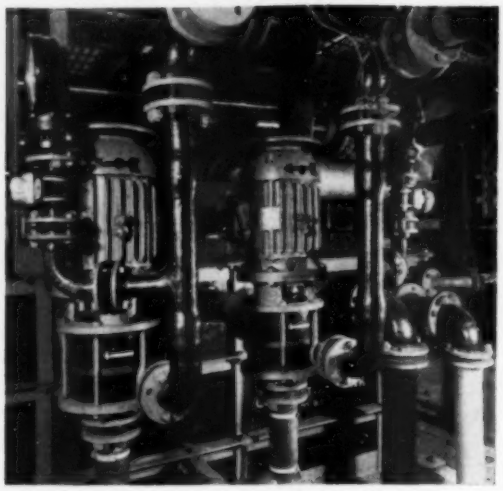
LOW-COST STAINLESS STEEL PIPE

The technique of helical welding is not new, but the metallurgical problems of applying the process to stainless steel have only recently been solved by a Birmingham company who are now making spirally welded pipe in stainless and nickel alloy steels.

The advantages of spiral welding are that the process brings straighter, cleaner, longer and lighter pipes. Automatic welding produces a bead of exceptional quality, and the pipe formed with micro-metric accuracy is of unlimited length, and above average straightness. The most important aspect, however, is the strength of the new pipe. Tensile tests indicate the added strength is due to the spiral formation, which, since the joint is at an angle to the stresses at the circumference, subjects the seam to only a fraction of the full tensile force. Additional strength means lighter gauge metals may be used.

Lighter metal and fewer joints make a less costly installation possible, and the makers claim that in some cases they can in fact quote prices less than an equivalent system in mild steel. This is possible, they say, because helically welded pipe has been "tied in" with the *Weltexa* method of prefabricating complete installations from standard parts. An excellent example of the Weltexa system is to be found at the International Synthetic Rubber Co. Ltd. plant at Hythe, where, because of the corrosive nature of the acid solutions employed, all pipes are in 18/8 chromium-nickel steel.

There is no doubt that a combination of these two techniques, spirally welded tube and prefabricated systems from standard parts, has brought down the cost of stainless steel pipeline installations and has made them far easier to install and maintain.



Keebush (reinforced Bakelite) piping on a chemical plant made by Kestners for Courtaulds and exported to Russia.

REINFORCED RESIN PIPES

While today the spotlight is on PVC and polythene for pipes, it is interesting to recall that nearly 30 years ago a reinforced Bakelite resin was introduced to the chemical industry in the form of a fan propeller for acid fumes. The material was called *Keebush* by the chairman and founder of the Kestner Co., Mr. Arthur Reavell. He spent a long time finding the right type of asbestos for reinforcing the resin and finally chose a Rhodesian type. Today there are many formulations of *Keebush*, some of general application for chemical work, others for specialised uses, so that the corrosive effects of acids, alkalis and such substances as fruit juices are successfully combatted. There seems to be no limit to the size of piping or ducting. Pipes are regularly made in sizes from ½ in. dia. and ducting up to 100 in.

Two or three years ago Kestners added *Keeglas* to their range of materials of construction. This is a glass fibre reinforced plastic of high strength and corrosion resistance. They also have a reinforced PVC formula which can be used for piping and ducting. A plant for nitric acid fume extraction was recently made of this.

Lately the company has supplied *Keebush* plant to Courtauld's Ltd. for export to Russia.

PIPING UP CHEMICAL PLANTS

(*Continued from page* 449)

perience of contractor. Where *real* confidence exists, this is in fact the most economical method, completely dispensing with the various contingencies for which provision has to be made in all others.

Some contractors offer an "all in" composite rate per hour applicable to all classes of labour, inclusive of all bonus payments, travelling time, welding sets and tools and lifting tackle. This provides a ready check on costs and performance and simplifies accounting procedure.

Antifoams. This word is nowadays generally synonymous with silicones. A folder containing the latest information on foam control comes from I.C.I., who make silicones at Ardeer, Scotland.

Preservatives. Four folders from I.C.I. discuss the uses of their *Topane* series of phenylphenol and phenylphenate antibacterials and preservatives in disinfectants, food, building materials and adhesives.

IRON TREATMENTS FOR PIG ANÆMIA

By Rudolph Seiden, Ch.E., D.Sc., F.A.I.C.

The author thinks that oral iron preparations are competing more strongly with parenteral preparations. But in many cases mixed therapy is needed—for example, a combined liver extract and iron preparation. British veterinary medicine manufacturers have taken the lead in this field.

THERE exist many types of anæmia, all of them characterised by fewer than the normal number of red blood cells; *i.e.*, a decrease of the quantity of hæmoglobin, the blood pigment. While pernicious anæmia is rare (if it exists at all in livestock), secondary anæmias—the results of some other, primary disease or abnormality—occur often among farm animals, particularly in baby pigs and the young of other species.[1] Secondary anæmias are often due to infestation with internal parasites, infectious diseases, hæmorrhages, scouring, nutritional anæmia, or iron deficiency anæmia—which is on the increase in baby pigs and other animals raised on concrete floors without access to soil. Iron anæmia is caused by improper or inadequate feeding, especially if the feed is deficient in iron and/or the trace elements copper (Cu) and cobalt (Co).

No animal can thrive, and many die, if chronically anæmic. There always has been a high mortality rate in baby pigs—in the 1940s, often 25% of the pigs farrowed died before they reached weaning age; of these, most were anæmic and many were farrowed by sows that had not been fed properly during the gestation period.[2] This situation has changed in the last few years, when parenterally administered iron became available; and indications are that another change in the prevention and treatment of baby pig anæmia is just now taking place. Before discussing this change in therapy, let us review the history of pig anæmia treatment.

Original research

For decades it was the custom to throw black dirt and sod with grass and grass roots into the pens of pregnant and nursing sows, particularly if weather or circumstances did not allow baby pigs to run on farm land and to eat solid food as early as possible. However, it was not until 1923 that causes and control of pig anæmia were investigated scientifically. In that year McGowan and Crichton[3] published an article on "The Effect of Deficiency of Iron in the Diet of Pigs." In 1931 Lintzel *et al.*, recommended the feeding of iron sulphate to sows before farrowing and to pigs soon after birth; and in 1936 Hart *et al.*, of the University of Wisconsin, found that (4%) Cu is needed to make (100%) elemental iron (Fe) effective in the treatment of secondary anæmias. These investigators also found that Co, nickel, manganese, zinc (and germanium) are hæmatopoietics (*i.e.* agents which affect the formation of blood cells). However, it took another 11 years before the first thorough research work was undertaken on the "Iron Metabolism in Piglet Anæmia." It was in 1947 when Venn *et al.*[4] published the results of their basic and still today unexcelled investigations. Venn and his associates proved that baby pigs need 7 mg. of Fe daily during the first three weeks of life, of which only 1 mg. Fe per day is made available to the suckling pig in the sow's milk. Thus the fast-growing pig, which at birth has a reserve of approximately 40 mg. Fe stored in its system, will very soon deplete the reserve and become anæmic, especially if raised on concrete.

In the 1880s drugs were administered intramuscularly for the first time—but it took 50 years to discover that the path of absorption depends on the size of the molecules of the injected substance. Drinker and Field[5] found in 1933 that small molecules, if administered intramuscularly, are absorbed directly into the blood stream, while larger ones enter first the lymphatic system. And Barnes and Trueta,[6] in 1941, proved this to be true for venoms and toxins by showing that those of a molecular weight of 20,000 or more are absorbed by the lymphatics, while those of a molecular weight of 5,000 enter directly into the blood stream.

Colloidal iron

The first application of these interesting findings to the treatment of pig anæmia was the colloidal iron product *Ferrovet* (Brit. Pat. 694,452 of *Crookes Laboratories*) which has been marketed in Great Britain since 1954 (in the U.S.A. the NDA (new drug application) became effective in 1960,* after millions of doses were used abroad). This product is prepared from a dialysed iron solution and sucrose (carbohydrate) and has a mean molecular weight of approximately 1400.

Iron-dextran

Another widely-used parenteral iron preparation of the carbohydrate group is the iron-dextran complex, also originally developed in Great Britain (by *Benger Laboratories* (U.S. Pat. 2,820,740)). There exist more than one iron-dextran complex patent in the U.S.A. and elsewhere, seemingly because more than one process allows its manufacture; also, there exist great differences in the molecule sizes of the complex which, according to the aforementioned findings, differ in the route of

* Haver-Lockhart negotiated for *Ferrovet* in 1958; when the FDA finally approved it, the market situation had deteriorated so making it impossible to sell the drug profitably in the U.S.A.

absorption after intramuscular injection. The original British product is supposed to have a molecule range of 10,000-20,000. The British-American *Armidexan*—in Germany known as *Myofer* (Hoechst) and *Ferrofort* (Veterinaria)—competes with others, seemingly of different molecule ranges, *e.g.* the American Pharmachem product (U.S. Pat. 2,885,393). If one compares claims made for the various parenteral preparations now available for veterinary use—and there are many; *e.g.*, the various iron dextrans; hydrogenated iron dextran (Nopco); iron saccharates (widely used in Europe); iron polysaccharide (Myzon); iron dextrin (Lederle, Merck); iron protein (diamond); peptonised iron (Specifics); ferric ammonium citrate (Haver-Lockhart; Squibb), etc.—one will find that even independent investigators at colleges do not come to unanimous evaluations: they may claim different preparations as the most effective ones. Reasons for the discrepancies are many—chiefly the fact that the tests are too often not performed in an identical manner; the breeds of pigs used differ as to management and feeding methods as well as feed; and even the analytical laboratory methods are not always of the same sensitivity.

Oral iron favoured

The pendulum is starting to swing back—the parenteral iron preparations containing 50, 75, 100, 110 mg. and maybe more elemental Fe per ml. no longer sell in the many millions of doses which were used annually in the late 1950s. Not only the discrepancies in claims made for them and/or the cost of the parenteral treatment are the causes for the changes taking place in the therapy of pig anæmia, but also—and probably more so—an important finding made by veterinarians and farmers, and substantiated more recently by independent investigators in different parts of the world: namely, that making oral iron available daily is a most efficient and very economical method of preventing and controlling anæmia in baby pigs!

The number of articles published since 1955 in veterinary and farm journals in all parts of the world on iron therapy is legion. If one reviews them critically and tries to analyse these reports and recommendations, one comes to the conclusion that parenteral iron therapy is valuable in many cases and places, but not always! It is also true that single oral dosages of iron, *e.g.* in form of reduced iron tablets, are not sufficient, even though this and other oral treatments were used for a long time before parenteral iron was introduced. The latter rarely, if ever, can compete with daily oral doses of iron given to baby pigs during the danger period (*i.e.* the first three weeks of life).

Many iron salts[7] have been made available—ferrous sulphate (copperas), ferrous carbonate, ferric ammonium citrate, ferric choline citrate, ferric chelate complex, ferric phosphate and pyrophosphate, ferric chloride, various iron oxides, etc. They are administered—often mixed with trace elements, vitamins, and other supportive ingredients—in form of tablets, powders, solutions, pastes, and now also as aerosols. The latter—*e.g.* the H-L Iron Bomb—replace the often sticky, messy and sometimes unsanitary liquids smeared cumbrously on the sows' udders.

W. J. Wilkie[8] of the South Australian Department of Agriculture gave proof that oral Fe, if made available at all times, gave better results than parenteral Fe when a second injection of the latter was not administered at the right time. Wilkie contends that a minute amount of elemental Fe—15 mg. or ¼ grain daily for the first 21 days of their lives—is all that is needed to prevent baby pig anæmia. In this connection, it is interesting to refer to a report by Becker *et al.*, of the University of Illinois, on their comparative study which led them to the conclusion that the survival rates of baby pigs receiving parenteral iron preparations were approximately identical, but did not reach the 100% mark established for the pigs which received Fe orally.

Mixed therapy

In closing, let us try to predict what the future of pig anæmia therapy may be. It is certain that parenteral iron therapy has its place in the veterinarian's armamentarium—but it is not the answer to all the questions concerning prevention and control of all types of anæmias befalling baby pigs raised anywhere and under every kind of management method. It took a number of years to find out this simple truth. That is the reason why oral iron is again being used more and more in the pig-raising areas everywhere. Yet, oral iron is not the answer to all the problems—there are many, many cases in which mixed therapy is needed. It must be remembered that pig anæmia is a secondary condition and that there are many baby-pig diseases which endanger the lives of the young animals even before symptoms of anæmia show up. To name only a few, I refer here to the so-called "baby pig disease" (a disturbance of the carbohydrate metabolism characterised by low blood sugar and glycogen content) and one of the greatest killers, baby-pig scours, which spreads fast and on some farms kills more than half of the pigs in the litter.

One of the most successful control measures for baby-pig scours, developed in Great Britain, is the injection of crude liver extracts. Thus, the idea of combining both liver extract and an Fe compound, particularly for the prevention of not only anæmia but also the often more dangerous scours, as originally established in H-L *Allane*, is rational. And because disease resistance and also growth rate are increased by liver extract and certain B-complex vitamins, these are now incorporated in many Fe-containing products, as are, occasionally, carbohydrates and trace elements. Such multiple-purpose products for either oral or parenteral administration will, I am sure, become more widely used.

And I also predict that preparations for oral use, made available *at all times* to baby pigs—particularly those raised on concrete floors—will have the preference of those who have to figure out which is the most economical control measure available to them.

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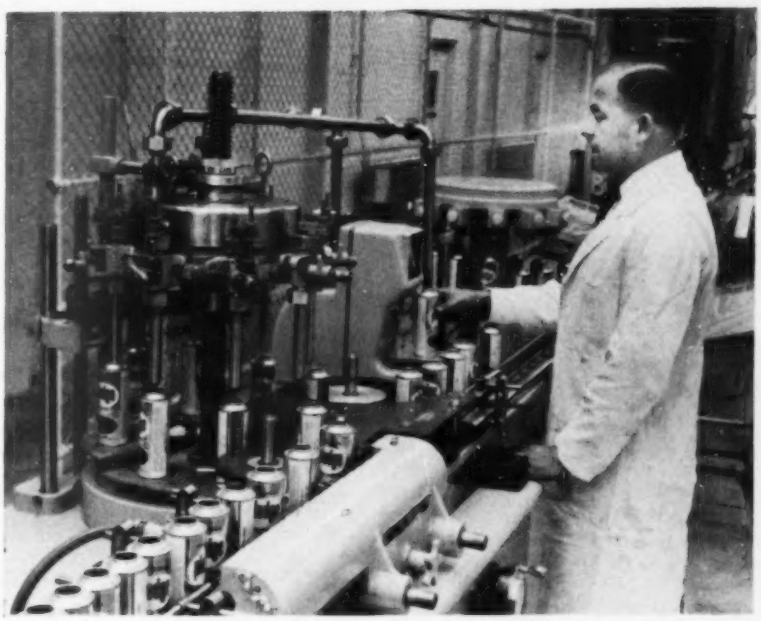
Press Button Packs—a New Plant at Bracknell

A NEW plant for the contract filling of aerosol packs has been installed at their Bracknell, Berks., factory by Aerosol Packaging Co. Ltd. It can fill 100,000 units a day or 25 million in a working year. APC aim to fill that number of aerosol units in 1961. Last year they filled a third of the aerosols marketed in Britain.

If U.S. trends are followed, by 1967-8 the British market may absorb 250 million aerosol units—about five per head of population.

APC was formerly part of the French Safca organisation. In January 1956 it was bought by the Tilling Group for £50,000, since when a great deal of money has been invested in premises and plants. The latest plant is the third major extension in a few years.

The development of the pressure pack has been extremely rapid in recent years and the range of products so marketed grows continuously. In MANUFACTURING CHEMIST, June 1961, we reported that insecticides and space sprays accounted for 40% of the 45 million aerosol units sold last year. Air fresheners took 20%; household products 19%; cosmetics and toilet goods 10%; mothproofers 7%; and industrial products 4%. Mr. M. N. Conville, A.P.C.'s managing director, grouped the products packaged by his company into five classes: cosmetics, household, insecticides and air fresheners, pharmaceutical and industrial, the first group being the largest. In the U.S. insecticides and room deodorants form the largest group and aerosol production totalled 670 million in 1960, compared with 45 million in the U.K.



Cans approaching the product filling machine are conveyed to a rotating segmented table. Container is automatically positioned under filling tube and as the table revolves, each segment is raised, offering container to tube. A measured quantity of the product is fed in and segment drops down. Container is fed back to belt and random weights are checked against a master sample.

Pressure pack production is a highly technical operation. A.P.C. employ a rotary pressure filling line designed and made in America, with baths and conveyors made by Metal Box. Each container is pressurised with a gas or propellent and considerations such as the type of propellent to be used, the ratio of propellent to product, design of valves and containers are taken into account.

The factory was extended in 1958-9 to include a new laboratory and can store. Now a new site has

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Left: Crimping machine seals the valve on to the container. Centre: Initial stages of production line, showing unscrambling of containers, batch identification coding machine, rotary product filling machine, purger which injects propellant to expel air, caps and valves insertion, rotary crimping machine, pressure filling machine and valve button fitting. Right: 250-gal. stainless steel tanks supported on weighbridges for mixing products.

Analysis ★ Skin Medicaments ★ Interferon

The British Pharmaceutical Conference was held at Portsmouth from September 18-22. The chairman, Dr. D. C. Garratt, opened the conference with an address entitled "Analysis analysed: A more rational approach to pharmaceutical control." The Conference Lecture was given by Dr. Alick Isaacs on "Interferon," and Skin Medication was the subject of the Symposium Session. In the Professional Sessions, the impact of restrictive practices legislation was reviewed by H. E. Chapman and the Joint Secretary of the Pharmaceutical Society, F. W. Adams, discussed the Report on the General Practice of Pharmacy. The Science Sessions included papers on various aspects of sterilisation, neuromuscular blocking agents, assay processes, the strength of compressed tablets, entrainment in stills, and the evaluation of modified aluminium hydroxides. The chairman's address, the Conference Lecture and the Symposium Session are summarised here by

S. J. Hopkins, F.P.S.

Analytical Advances and Drug Control

ANALYSIS has now broken out of its once restricted sphere, and its phenomenal expansion, due to new instrumental methods, has coincided with the necessity for more rigorous control of the potent drugs now in use. Modern methods of manufacture and new materials for containers also increase the responsibility of the analyst. Such strict control is expensive and is a factor in the cost of the National Health Service, and the question arises whether we are making the best use of our analytical resources. Some misleading figures of the cost have been quoted, but a satisfactory estimate can be obtained by expressing the analytical costs as a percentage of the total production costs. During the past five years this has increased by 1% and is due mainly to the cost of analysts, who are at a premium. This acute shortage is due to past lack of encouragement to chemists to take up analysis, which is now being remedied slowly by the establishment of Chairs of Analytical Chemistry. Pharmaceutical analysis is a specialised part of this field and pharmacists should not allow this branch to remain largely in the hands of non-pharmacists.

Manpower in pharmaceutical laboratories has been saved by replacing chemical methods with physical techniques, and the use of emission spectrography, flame photometry, fluorescence spectroscopy have speeded up much routine analysis. With these improvements it is important to ensure that the tests are worthwhile, as there is little justification for many of the assays applied to synthetic drugs. In some cases the purity figures are meaningless, and the measurement of ultra-violet spectrophotometry as a test of purity is unrealistic unless standard material is available for comparison. There is urgent need for a national collection of substances of which the amounts of impurities are known accurately. There is also a need for more specific tests of identity and assay, and more important than traces of lead and arsenic are residues of highly toxic catalysts. Difficulties also arise with formulated products, and common sense must be shown in assessing the precision of assays and the interpretation of borderline results.

There are also hidden costs which should be investigated. Some can be discovered by work-study methods, others can be reduced by the use of less expensive solvents. Working time can be saved by replacing gravimetric methods by titration with EDTA. Paper-chromatography can aid in avoiding bio-assay of rejected samples of insulin, and the relative merit of alternative tests is also worth consideration. The elimination of assays already done is another factor. This applies particularly to the quality control of purchases, which repeats work carried out by the supplier. Any material supplied by a reputable house has already been tested, and such companies should accept each other's assays. Such a system, already approved in principle, is already working in some instances, and could be extended to cover a wide range of drugs.

Control of drugs

A revision of the legislation concerning medicines is contemplated, and this may be an opportunity for a general overhaul of the control of drugs. A logical course of control of a new drug would include statement of therapeutic applications, toxicity, clinical trials, fixing of standards and control to those standards, and should be regulated by the General Medical Council and the Ministry of Health. Ideally, the standard should be fixed before the drug appears on the market. This should not be difficult, as the manufacturer will have much information, and many official monographs are already based on data supplied by manufacturers. A suitable scheme could be introduced in a manner similar to the Agricultural Chemicals Approval Scheme of the Ministry of Agriculture and Fisheries. Such a system, begun on a voluntary

basis, could be made obligatory later, and cover imported as well as home produced compounds. British manufacturers are already familiar with the system in reverse, as exported drugs must usually be accompanied by extensive information.

At present full control over available drugs is lacking. Samples taken under the Food and Drugs Act and for testing under the National Health Service are limited mainly to popular galenicals and standard drugs. Few proprietary preparations are tested, and it is suggested that the control of drugs should be taken out of the Food and Drugs Act and incorporated in a new Act based on Sections 11, 12 and 13 of the Pharmacy and Medicines Act. An advisory body would be required to make recommendations under the Act, and specialised, regional laboratories required for the necessary testing. These laboratories should be responsible directly to the Ministry of Health and should also control imported drugs. As proof of competence as a public analyst under this scheme, a special diploma in drug analysis from the Pharmaceutical Society or the Royal Institute of Chemistry could be demanded, and such a demand would be in keeping with the need for courses in pharmaceutical analysis.

Symposium on Skin Medication

This was opened by Dr. F. J. Ebling, who discussed topical medication in relation to skin physiology. The skin was once a neglected organ, but experimental dermatology is expanding and developing and further advances can be expected. But much remains, as the way the corticosteroids work, why hydrocortisone is effective but the related cortisone is not, how histamine is held or released from cells, are still debatable points.

He was followed by Dr. A. Jarrett, who reviewed the ways in which skin function can become abnormal, and summarised the blistering diseases, infective skin conditions, disorders of the sebaceous glands, and a group of various conditions referred to as dermal disorders.

Formulation of skin preparations

The pharmaceutical formulation of preparations for skin medication was the subject of a valuable paper by J. W. Hadgraft. In this paper it was pointed out that no single preparation or base could meet all the criteria of a dermatological base, but a range of preparations could now be formulated for selection according to need. The importance of simple formulation was noted, since the fewer ingredients the less risk of causing skin sensitisation or interference with the action of the medicament. More precise knowledge of the effects of topically-applied products is needed, as many preparations are used mainly for traditional reasons.

Lotions

Lotions are usually simple, but solubility problems occur, as with hydrocortisone, which can be suspended with a combination of cetomacrogol and self-emulsifying monostearin, or dissolved in a water-miscible vehicle such as liquid macrogol. Pharmaceutically employed suspending agents such as bentonite compare unfavourably with related cosmetic products, and more research is needed. Permanent suspensions with maximum flow properties can be formulated by using hydrophilic colloids with a high yield value : apparent viscosity ratio. By controlled homogenisation, solutions of gums such as tragacanth can be prepared with a range of stability characteristics. The influence of other ingredients on suspending agents can also be considerable, as the addition of sorbitol or glycerol to methylcellulose solutions may convert an easily pourable fluid into a semisolid gel.

Ointments

Ointments can no longer be divided into emollient and protective types, and glycerol, a traditional emollient, increases the loss of water from the skin. Mineral oil products are not absorbed, have the advantages of chemical stability, but the composition of soft paraffin cannot be defined, and the substance is variable in consistency. This effect can be reduced by combining it with both hard and liquid paraffins as in paraffin ointment. Some proprietary mineral waxes have better blending powers than hard paraffin owing to their "amorphous" or "microcrystalline" structure, and produce homogeneous mixtures with both mineral and vegetable oils. Some such mixtures possess thixotropic properties.

Examination of wax-thickened mineral oils has led to their use as ointment bases. A proprietary base is prepared by dissolving polyethylene in mineral oil, and cooling the solution very rapidly. The polyethylene is precipitated in an amorphous form, and the resulting base is non-reactive, of reliable consistency and of stable viscosity over a temperature range of 5°-45°. Wool fat is absorbed better than mineral oil products, and the acceptability can be improved by mixture with soft paraffin as in simple ointment. Derivatives of wool fat, such as wool alcohols, can be combined with paraffins to produce hydrophilic bases. These alcohols undergo autoxidation during storage, but this may be prevented by the addition of butylated hydroxyanisole (500 p.p.m.). Hydrogenation of wool fat results in a solid white wax (m.p. *c.* 50°), and when formulated with liquid paraffin produces a smooth base, less sticky than unmodified wool fat bases. Other modifications result from the interaction of wool fat and ethylene oxide, and the wax so produced has some of the properties of wool fat combined with solubility in water, and is of dermatological interest.

Vegetable oils

Vegetable oils can also be modified, and by replacing some of the fatty acid groups in the triglycerides the acetoglycerides can be obtained. Depending on the oil and degree of acetylation, mobile oily liquids, semisolids and solid waxes can be obtained. These products have a microcrystalline structure, and when mixed with oils and waxes the preparations have a stable consistency over a wide range of temperatures. Skin penetration should be good, but no tests have yet been reported.

Synthetic esters of fatty acids are already used in cosmetics and have a number of advantages. Isopropyl myristate is an oil of this type, and when mixed with paraffins reduces viscosity and improves the skin spreading properties. The palmitate and palmitate-stearate esters are more viscous. The addition of this kind of substance to conventional bases could produce ointments more

pleasant in use, less occlusive, and cause less interference with the normal movement of water at the skin surface.

Emulsification

Emulsified bases are widely used, but emulsification does not increase skin penetration. The rate of release of contained medicaments is affected by the phase of the base in which they are soluble, but the concentration of the drug in the residual film on the skin will be greater than in the original product. This may be an explanation of the increased effect of emulsified bases over oily products.

Aqueous creams are formulated with surface-active agents, which may be anionic, cationic or non-ionic compounds, and for reasons of stability are used in association with a substance such as cetostearyl alcohol which produces a stable interfacial film. Electrolytic considerations govern the use of anionic and cationic surface-active agents, but the non-ionic compounds have a wider range of compatibility. These agents exhibit both hydrophilic and lipophilic properties, and by varying the proportions of oil-soluble and water-soluble compounds a range of emulsifying agents of varying hydrophile-lipophile balance can be obtained. A relationship between this balance and the spreading coefficient has been found, and for stability the agent used must provide the least spread consistent with emulsifying balance. A practical method of test and selection of agent is known, and could be applied in the investigation of stability of dermatological creams.

The preservation of these aqueous creams, particularly those containing non-ionic agents, presents difficulties. Methyl hydroxybenzoate is widely used, but its effectiveness is reduced by its solubility in the emulsifying agent. This may be offset by the addition of propylene glycol, which increases the solubility of the preservative in the aqueous phase.

Aerosols

Aerosols are now being used for applying medicaments to the skin, and the possibility of some of the propellant remaining after application to the skin requires consideration. Alternative propellants, such as carbon dioxide, may increase wastage and therefore costs. In general, aerosols have certain advantages, as the product can be kept in a sterile condition, applied by a no-touch technique, and permit adequate coverage of large areas with minimum amounts of drug. The full effect and precise value of aerosols, as well as the effects of various formulations of other forms of topically applied medicaments, still await further study.

Prospects for Interferon

Dr. A. Isaacs gave the Conference Lecture on Interferon. He said that research in an academic field may lead to practical prospects, and research on interferon is an exciting example. It has been known for 25 years that virus-infected cells acquire a resistance to other viruses, and later it was shown that a killed virus might retain the ability to interfere with the growth of other viruses, but not their entry into the cell. In 1957 a viral inhibitory substance (interferon) was separated from cells treated with killed virus, and appears to be produced by the cells as a cellular response to infection. Interferon is liberated spontaneously and may enter other cells and protect them, and may play some part in the defence of the body against virus infection. Resistance to infection with virus may include recovery from a first infection and a prevention of a second infection. The significance of antibody in recovery is not clear, and other mechanisms, including interferon, play an important part. This is supported by the fact that cortisone can inhibit the antiviral action of interferon, and it is known that patients under treatment with cortisone are a special risk from chickenpox virus infection.

Interferon is a protein of M.W. about 63,000, and evidence suggests that it acts by inhibiting the synthesis of viral nucleic acid or protein without significantly inhibiting the formation of nucleic acid required by the normal cell. This distinction is a very selective one, and it may be that "foreign" proteins are built up by a different process than that for normal cell protein, and that interferon blocks one process but not the other. Much further investigation will be necessary on this, and also on the function of interferon in the normal cell. Interferon has very little antiviral action in very young cells and in cancer cells, and may be concerned indirectly in the differentiation of young cells. Cancer cells may be regarded as cells that have escaped from the differentiation system, and speculation suggests a number of experiments on this aspect of interferon. If the compound also plays a part in normal recovery from viral infection, it is logical to attempt to use it to improve the natural mechanism. This reasoning has led the Medical Research Council to collaborate with three pharmaceutical firms in examining the problem. Animal experiments have been encouraging, but a long investigation will be required to improve yields of interferon and study its use in human viral infections. It is to be hoped that this interesting partnership between the M.R.C. and British pharmaceutical industry will be extended in future to many other fields.

PRESS BUTTON PACKS

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been developed at Bracknell to accommodate a 24,000 sq. ft. storage building and a 5,000 sq. ft. drum store, with a further 3 acres for additional projects.

The ubiquitous press button container, now used for such diverse purposes as control of foot rot in sheep, dry cleaners, garden sprays, cold reliefs, shoe polish, dog shampoos, toothpaste, hair lacquers, and for several industrial applications, plainly has an expanding future. The latest innovation in America is an areosol packed starch which is dispensed at the ironing board. A.P.C., aware of their responsibilities in providing an efficient and economic contract packaging service, believe that a big market exists in the U.K. for this and many more aerosols.

Chemical plant and equipment. A new leaflet from Plenty and Son Ltd. illustrates examples of the range of equipment manufactured and details of installations and services offered. Leaflets describing pumps, filters, etc., in detail are available.

Synthetic Steroids of Medicinal Interest

By J. D. P. Graham,* M.D., F.R.C.P.(E).

In the first part of his article published last month, Dr. Graham discussed the synthetic sex hormones and adreno corticoids. He concludes the article with a description of methods of synthesising sex hormones.

Part 2. Methods of Synthesis

SYNTHESIS of steroid hormones is necessary if they are to be available in any quantity, since they are not stored in any organ from which they might be extracted; 50,000 sows' ovaries only yielded 20 mg. of progesterone in one such attempt. Water-soluble conjugates of œstrogens may be extracted from such sources as horse urine, but the other hormones are not present in large enough quantity to make the matter practicable.

There are two general categories of preparation:

(*a*) *a total synthesis* from such starting materials as acetic acid. These syntheses have been achieved in all or almost all cases but are too expensive to be useful;

(*b*) *partial syntheses* where the starting material is a natural steroid. A number of these which are at present of commercial importance are listed in Table 3. The individual choice depends on availability of the source material, *e.g.* cholesterol and bile acids from a large meat-packing industry, diosgenin from Mexican yam which grows wild there, hecogenin from sisal, ergosterol from yeast, as well as consideration of the desired end product. If the hormone does not contain a substituent on C-17 and no functional group in ring C, *e.g.* progesterone, it can be prepared from a sterol.

The key step in the production of methyltestosterone or ethinylœstradiol from cholesterol is drastic oxidation with chromium trioxide to give a small but valuable yield of a 17-keto steroid by removal of the side chain. If, however, the product wanted has a substituent at C-17, *e.g.* cortisol, this approach fails because the addition reaction on the 17-carbonyl group necessary to rebuild the side chain invariably produces the inactive enantiomorph.

Table 3

SYNTHESIS OF STEROID HORMONES

Starting material	*Source*	*End product*
Cholesterol	Brain	Œstradiol
Stigmasterol	Soya bean	Cortisol
Ergosterol	Yeast	Cortisol
Desoxycholic acid	Bile	Cortisol
Diosgenin	Mexican yam	Progesterones
Hecogenin	Sisal	Cortisol
Sarmentogenin	Strophanthus	Cortisol

It is preferable to use a starting material which possesses a functional group in the side chain which includes double bonds as in stigmasterol and ergosterol or a carboxyl group as in the bile acids. A further point of great significance is whether or not the final product must have an 11-OH function.

As a starting material sarmentogenin, a cardio-active glycosidic steroid obtained from the seeds of certain West African plants, is excellent since it already has an 11-*a*-OH group, but the material is very scarce. It is more usual to utilise such steroids as hecogenin or bile acids which have an oxygen at C-12 and to shift it to C-11. The starting materials for a chemical method must have at least one double bond in ring B, hence the former dominant rôle of ergosterol (Fig. 1, 5 = 6; 22 = 23; 21,26,27,28-$(CH_3)_4$) which is easy to produce in mass from culture of yeast. The vital shift to 11-oxygen may also be performed by fermentation, in which case the initial chemical steps are not necessary and the starting material need not be an unsaturated steroid.

The details of the preferred methods which give the best yields and are most economic are jealously guarded manufacturing secrets, but the following syntheses are in use and are successful.

* Dept. of Materia Medica and Pharmacology, University of Wales.

(*a*) Sex Hormones from cholesterol. (The skeleton of Fig. 1 with a 5,6-double bond in ring B and no C-28 group.)

If the double bond in the cholesterol chain is protected by conversion to the 5,6-dibromo derivative, drastic oxidation with chromium trioxide yields dihydroepiandrosterone (the skeleton of Fig. 1 with a 5,6-double bond in ring B and 17-keto group in place of the side chain). This is a useful intermediate for several syntheses. Ni reduction gives 5-androstene-3,17-β-diol; from this may be prepared the 17-benzoate. If this product is subjected firstly to oxidation (Oppenauer method) and hydrolysed, testosterone (Table 1) results. The chemical conversion from dihydroepisterone has been largely replaced by fermentation.

Reduction of the diacetate of 5-androstene-3,17-diol followed by a controlled partial hydrolysis yields the 17-acetate of androstane-3,17-diol which is easily oxidised to the 3-ketone (Fig. 1 with 3 = 0 and 17-OH, no side chain). Bromination of this ketone to the 2,2-dibromo derivative and isomerisation with acids to the 2,4-dibromo form follows. Dehydrobromination yields 1,4-androstadien-17-ol-3-one. If this is heated with a suitable hydrogenating agent methane is eliminated from ring A and œstradiol (Table 1) is formed.

(*b*) Diethylstilbœstrol (Table 1) may be prepared by the condensation of two moles of anethole hydrobromide ($PhOCH_3.CHBr.Et$) with sodamide in liquid ammonia. If the intermediate so formed is pyrolised in alkali diethylstilbœstrol is formed in good yield. Chlorotrianesine may be formed from the same starting material, whereas a naphthalene is used for methallenestril.

(*c*) Progesterones from sterol. Ergosterol (Fig. 1 with two double

bonds in ring B and one in the side chain between C-22 and C-23) is easily obtained by culture of yeast. It may be subjected to Oppenauer oxidation to yield ergosterone (Fig. 1 with 3 = 0, double bonds at carbons 4, 5 and 7, 8). This is isomerised through the enol ether to the di-unsaturated ketone with double bonds at 4, 5 and 6, 7. Reduction is then carried out by Li in ammonia to the monosaturated ketone (double bond in ring A at 4, 5 only). The side chain may then be removed by ozone to form an aldehyde. This can be converted to progesterone via the enamine or the enol ether. The overall yield of progesterone, which is itself an intermediate for progestogens or for adrenocorticoids is approximately 37% so that this synthesis is much favoured.

Progesterone has also been prepared from stigmasterol, which is found in soya bean oil, by degradation of the side chain and Oppenauer oxidation. However, a much less tedious process which has largely displaced this synthesis is that which starts with diosgenin,[2] a sapogenin obtained in fairly high yield from the wild Mexican yam. Diosgenin has a double bond in ring B and an 11-carbon ring system in place of the side chain of Fig. 1. When treated with acetic anhydride it yields an ester which may be drastically oxidised with chromium trioxide to give 5,6-pregnadien-3-ol-20-one on hydrolysis. This can be reduced to 5-pregnen-3-ol-20-one which has been dealt with above as an important intermediate. Half the sex hormones are made this way.

Progesterone can be hydroxylated at carbon 11 by a fermentation process so that these ways of producing it are of great commercial significance as a source of pregnancy hormone, of oral contraceptives and of adrenal steroids.

Adrenal steroids

(*a*) From bile acids. Cortisone was first produced from desoxycholic acid.[3] There are five main steps involved, *viz.*:

(1) Shift of the oxygen from C12 to C11 to form 11-ketolithocholic acid. This vital procedure has been studied intensively and there are a number of methods in use, some very complex. In one a double bond is introduced at C-9,11 by treatment with selenium dioxide and the 12-keto group removed by the Huang-Minlon procedure. The double bond is epoxidised. Drastic treatment with chromium trioxide gives 3,9-oxido-11-ketone. When it is brominated the product is a 3-ketone which is readily converted to 11-ketolithocholic acid (Fig. 1 with 11 = 0 and 24-COOH).

(2) Degradation of the side chain to yield pregnan-3-ol-11,20-dione. The Barbier-Wieland method is applied once to yield a 23-unsaturated compound which is converted into a 20,23-diene by standard methods. This product is converted to 20-ketone by ozone, or the diene can be reacted with N-bromosuccinimide, then with acetate and finally ozone to yield the 21-acetoxy-20-ketone.

(3) Introduction of a 17-OH group is achieved by means of a double bond at C-17 and oxidation of this ethylene linkage. A 20-double bond is introduced through the 20-cyanohydrin which then dehydrates to the unsaturated nitrile. This is reacted with osmium and the ester hydrolysed to give the 17,20-dihydroxy-20-nitrile. This spontaneously loses HCN to regenerate the 20-carbonyl group;

(4) Introduction of the 21-OH. This can be achieved immediately after the last through the 21-bromo derivative. There are shorter methods for the preceding steps;[4]

(5) Introduction of the 4,5-double bond by formation of the 2,4-dinitrophenylhydrazone of the 3-ketone or the semicarbazone. Bromination and debromination proceed well and the dinitrophenyl can then be removed by treatment with pyruvic acid. Thus 4,5-dihydrocortisone is converted to cortisone.

(*b*) From sterols. Ergosterol or stigmasterol (Table 3) may be converted to cortisone by similar processes to the above. Steps (3) and (4) are the same. As there is a double bond at C-22 in sterols two ozonisations are needed, the first to 22-aldehyde which is converted to the enamine and again treated with ozone. Step (1) is the most difficult. Chemical methods utilise a double bond in ring B as a means to introduce an oxygen atom on C-11 or a 9,11-double bond which can be oxygenated. Thus 7-ketocholesterol may be converted by bromination - dehydrobromination to the 8-dehydro derivative and further to the 11-ketone by chromium trioxide. This method does not work with ergosterol. For this sterol it is better to utilise a 9,11-double bond obtained by the action of mercuric acetate on the corresponding 7-unsaturated compound to yield a 7,9-diene system. To this is applied a peracid[5]—benzoic, for example—to yield 9,11-epoxide. Repeated isomerisations restore the natural configuration (9-α-H) and the 7-double bond is conjugated with 11-carbonyl and reduced to the 11-ketone by Li-ammonia technique. If the starting material is diosgenin the 5,9,11-triene system may be subjected to treatment with peracid, having been prepared from 9,11-diene bearing a 5-α-hydroxyl group. This has the advantage that the ultimate 11-ketone does not possess a 5-α-H (A/B *trans*). The performance of step 5 is as previously described. The product from other sterols does not respond to this technique for stereochemical reasons and complex steps are necessary to get the 4,5-bond.

(*c*) From progesterone. This steroid can easily be made in bulk as described. If it is given as substrate in deep culture of a mould *Mucorales rhizopus* the 11-α-hydroxylation is performed biosynthetically in high yield and cortisol may be formed in only three steps. A number of other fungi have been isolated which carry out all or almost all of the difficult chemical conversions summarised above. They are listed in Table 4, from which may be seen how important is progesterone. The combined use of chemical and biosynthetic processes is the basis of most bulk commercial syntheses.

(*d*) From sapogenins.[6] The

Table 4

BIOSYNTHETIC CONVERSIONS IN STEROID SYNTHESIS

Organism	*Substrate*	*Product or Effect*
M. rhizopus	Progesterone	11-α-hydroxylation
O. herpotrichus	Progesterone	11-desoxycorticosterone
C. lunata	D.O.C.	Corticosterone
T. roseum	Corticosterone	Cortisol
Fusarium sp.	Progesterone	Œstrone
Aspergilli sp.	Progesterone	4-androstene-3,17-dione
Yeast	4-androstene-3,17-dione	Testosterone
Penicillium sp.	21-desoxy-aldosterone	Aldosterone
C. lunata	9-unsaturated steroids	9,11-Epoxides.

carbon skeleton of these natural detergent-like materials is the same as cholesterol, the side chain is replaced by a cyclic ketal system. This may be ruptured by acetic anhydride. This is the key reaction in their utilisation as steroids because the double bond formed between 20,21 is oxidisable to a 20-ketone, and a 16-double bond is formed at the same time. From it 17-hydroxylation may be performed through epoxide. Hecogenin is 12-keto-5-α-6-dihydrodiosgenin (Table 3) and the conversion to corticoids follows the standard routes described.

(*e*) From cardiac glycosides. The aglycone of the digitalis-like compounds is steroid in structure and may have a 21-OH group. One of them, sarmentogenin, also has an 11-α-OH and is of the normal configuration. Such a starting material for the synthesis of cortisone is obviously of great value, but it is scarce.

Analogues.[7] There is room only to mention the preparation of prednisolone from cortisol by selenium dioxide treatment, and the preparation of 9-α-fluoro-cortisol. The 9- unsaturated compound is converted microbiologically to the 9,11-epoxide which is treated with hydrogen fluoride to yield the 9α-F-11β-OH compound. The introduction of a 16β-methyl group before the elaboration of the side chain gives the valuable dexomethosane.

Spirolactones.[8] Once the precise structure and function of a substance of biological importance is known, it should be possible to construct a competitive antagonist by modification of its molecule. Spirolactones, *e.g.* 3-(3 = 0 -7α-acetylthio - 17βOH - 4 - androsten - 17α-yl)-propionic acid-α lactone antagonise the effect of aldosterone in causing reabsorption of $Na^{\oplus}$. They are of value in any condition complicated by retention of salt and water, *e.g.* heart failure, high blood pressure or œdema.

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AEROSOL POWDER FORMULATIONS

D. C. Geary of the Union Carbide Chemicals Co. lectured recently on the subject of aerosol powders before the Chemical Specialties Manufacturers Association. Among the formulations he suggested were the following (all figures given in % weight):

TOOTHPOWDER

Dicalcium phosphate anhydrous	2·93
Dicalcium phosphate dihydrate	26·34
Santocel 54	1·54
Klearol (inert)	2·43
Span 85	0·69
Tween 80	0·39
Propellant 12/11(50/50)	65·68
	100·00

ANTIPERSPIRANT

Chlorhydrol	31·28
Santocel 54	1·05
R-45 oil (inert)	2·37
Hexachlorophene	0·27
Span 85	0·66
Tween 80	0·43
Propellant 12/11(50/50)	63·94
	100·00

INSECTICIDE

Sevin (technical grade 50 microns)	22·48
Santocel 54	1·73
Blandol (inert)	5·65
Span 85	1·34
Propellant 12/11(50/50)	68·80
	100·00

TOILET POWDERS

	Body	*Foot*
Italian talc	33·04	32·96
Santocel 54	1·01	0·69
Zinc stearate	—	0·66
Hexachlorophene	0·26	—
Dichlorophene	—	0·26
Carnation oil (inert)	2·14	—
Klearol (inert)	—	2·33
Span 85	0·86	1·01
Propellant 12/11(50/50)	62·69	62·09
	100·00	100·00

Mixers. The Lightnin Mixers process industries catalogue gives a picture of the range of equipment offered to many industries for fluid mixing and agitation. It contains further details of the new side-entry mixers.

TABLET MAKING

(*Continued from page* 446)

suction and brushing points—are attached to the machine to prevent carry-over of specks of one layer to the other. A good granule with plenty of " bite " is necessary for the best results, and an experienced machine operator is needed more in this than in conventional compression work. Similar points apply to cored tablet operations.

(c) Tacky materials. There is a limit to what can be done with these. One of the commonest methods was to use calcium phosphate as an absorbent, but newer materials, various physical forms of calcium silicate and silicic acid are better (*Aerosil*, *Calflo*, etc.).

Wherever possible a better physical form of the drug should be looked for; often another chemical derivative may be obtained which is more suitable.

(d) Direct compression of powders. It is often possible to avoid an intermediate granulation operation if the powder is coarse and has some reasonable flow properties. The die clearance should be larger than usual, and if a rotary machine is used the bottom punches should be locked to prevent rotation. This latter step is often useful also when a tablet tends to cap and it cannot be improved by other methods. It avoids any twisting action which tends to disrupt the tablet. Good lubrication is of course required. The new forced feed mechanism being fitted to some high-speed rotary machines facilitates this type of operation greatly and in some cases relatively fine powders can be compressed at one operation with this type of feed.

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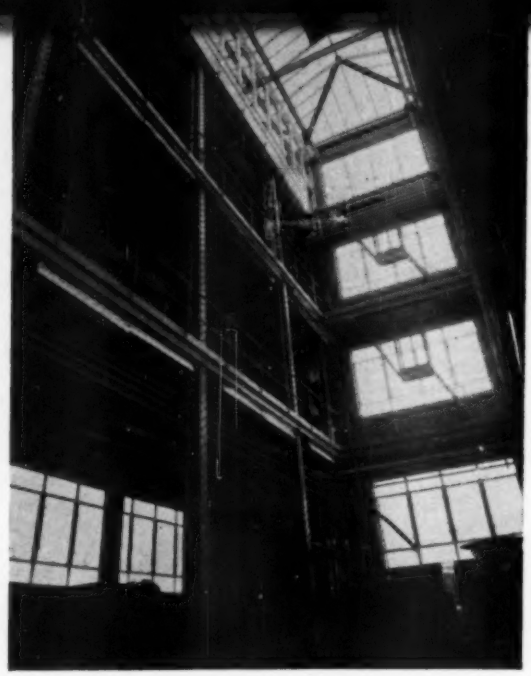


Left: Crosfield's new technical centre overlooks the Mersey. Right: The four-storey pilot plant.

New Centre for Research on Silicates—Chemical Industry's Maid-of-All-Work

THE NEW TECHNICAL CENTRE opened at Warrington recently by Joseph Crosfield and Sons Ltd. covers an area of 17,000 sq. ft. and embraces a vast range of silicates research and development projects. The centre, consisting of two main blocks of three and four storeys connected by a covered bridge joining the upper floors, brings under one roof, research, production development, quality control and technical sales service departments. Thus basic development of new materials, processes and techniques is closely linked to the practical requirements of the user, enabling industry to implement research at every step.

Since installing their first silicate furnace in 1895, Crosfields have developed and commercially produced sodium silicate and its derivatives for application in many fields: abrasives, industrial detergents, soaps, factory cleaning, dyestuffs, chemicals, insecticides, water softening and purification, hydrogenation, glass, pharmaceuticals, cosmetics and organic liquids, among many more. Today Crosfields are responsible for 70% of the national output of silicates.

Location and design

The new buildings are based on the foundations of a former wharf warehouse on the Lancashire side of the Mersey. The smaller of the two blocks houses the reception and administrative offices, library, conference room and general facilities. The main block contains seven separate research laboratories, together with ancillary equipment and service rooms and a large central pilot plant area.

Apparatus and equipment

Much of the apparatus is unique, having been designed to the requirements of the various research teams, enabling radioactive tracer, X-ray, thermogravimetric, spectrographic and other physico-chemical techniques to be used. The development of ultra-fine powders, largely depending on the ability to measure particle size distribution accurately, is facilitated by the use of the Bostock sedimentation balance, and a more sophisticated instrument, the Coulter counter, is used to give absolute counts of particles in a suspension. One of the most advanced instruments used is the Pye argon chromatograph, which separates organic mixtures into their component parts. Other items of equipment in daily use include the flame photometer, another sensitive impurity detector, and a large array of special laboratory apparatus, much of it developed and built in the Centre's own glass workshop. One interesting item is a bank of titration burettes mounted on an illuminated panel for accurate and rapid reading.

Technical sales service

The instruments and equipment are not reserved exclusively for research purposes. Much of the normal bulk output of the Crosfield plant must be prepared to pharmaceutical standards of purity and the chemical laboratory carries out routine analyses as well as normal quality control procedures. Laboratory facilities on the spot also enable Crosfield's technical service to solve user's problems.

This technical sales service links user industries to basic research and provides an invaluable feed-back of customers' information to the research teams. One of the department's laboratories embodies a special water supply system which can reproduce any required degree of hardness and the effects of local dosing practice.

Development

The product and process development department is responsible for the translation of techniques developed by the research section on a pilot plant scale to full-scale production methods. Besides work on the design and erection of new plants, improvements and modifications to existing plant are undertaken, and a close liaison between technical sales, research and development departments is maintained.

Quality control

Quality control, maintaining the highest standards, both in raw materials and throughout every stage of processing, is the responsibility of the chief chemist's department. Emphasis here is on process, assuming that strict process control ensures product satisfaction.

PERFUMERY and Essential Oils

By B. H. Kingston, B.Sc.

Citrus oils evaluation • Bergamot adulteration • Aromatic chemicals from pinene • Essential oils and aromatics solubilities • Perfume fixatives Aldehydes

Lemon oil

THE evaluation of citrus oils and the nature of the minor constituents is receiving increasing attention with the advent of newer analytical techniques. The difficulties of separating the terpenes completely have largely been overcome by selective chromatographic deterpenation, using a genuine cold-pressed Californian lemon oil: d_{20}^{20} 0·852, n_D^{20} 1·4749. The method,[1] which is a modification of the Kirchner-Miller technique, involves shaking a *n*-pentane solution of the oil with freshly-dried silicic acid. The latter, which absorbs the oxygenated compounds, is separated by filtration and washed with solvent. The O-compounds are finally regenerated with absolute ethanol. Gas/liquid chromatography (GLC) of the terpene filtrate showed 12 distinct peaks, of which the following were identified:

	%		%
α-Pinene ..	2·52	Terpinolene	0·14
β-Pinene ..	20·69	*d*-Limonene	66·59
Camphene ..	0·08	γ-Terpinene	6·88
Myrcene ..	1·28	*p*-Cymene ..	1·68
Unknown	0·14%		

No cadinene, bisabolene or β-phellandrene could be detected. The oxygenated compounds,[2] representing 4% of the original oil, comprised 23 different components. Of these, 13 have been reported previously as occurring in Italian oils. In addition, methyl heptenone, octyl acetate, citronellyl acetate and *n*-undecanal were definitely identified. The mixture also probably contained small amounts of *n*-decyl acetate and linalyl propionate.

The techniques used in this work have also been extended to the *evaluation* of straight and terpeneless lemon oils.[3] Tests on straight commercial oils from seven sources showed the presence of 8·5-10% oxygenated compounds, while oils freshly prepared from lemon peel yielded as much as 19% oxygenated fraction. In confirmation of previous work, results also showed that the proportion of citral-α is higher in Sicilian oils than in Californian and Nigerian oils. Deterioration of lemon oils by autoxidation results in the production of OH compounds and loss of aldehydes. Infra-red spectra have been used to assess the extent of this oxidation by measuring the ratio of the peak height at 2·95μ (—OH) to that at 5·95μ (—CO aldehyde), which is known as the "Deterioration Index." The value of the index usually lies between 0·15 and 0·20 for most fresh oils and in any case should never exceed 0·30. The use of i.r. spectra for the diagnostic assessment of lemon oils is also useful for detecting adulteration, especially in the 8-9μ region. While genuine oils have strong bands at 8·13, 8·40, 8·70 and 8·91μ, these are missing in most adulterated oils but are replaced by a band at 8·25μ. The latter oils also show strong absorption in the region 13-15μ.

Bergamot and murcott oil

Adulteration of bergamot oil is well known. Apart from lemon terpenes, linalyl acetate, etc., *p*-cymene and methyl carbitol have also been used as adulterants. A more accurate evaluation of the quality of this oil involves the use of spectrophotometric and GLC analysis.[4] For genuine oils, the specific extinction coefficient at 312·5 mμ absorption maximum (due to bergaptene) varies from 10-13. In diluted oils this value is proportionally reduced, depending on the amount of original oil present. Adulteration with terpenes may be detected by measuring the i.r. absorbance ratio at 12·00μ and 12·52μ. Values significantly below 0·9 suggest adulteration, whereas in genuine oils the ratios fall between 0·9 and 1·14. This can be confirmed by quantitative GLC measurements using a carbowax column at 175°C. The main components of natural bergamot oil should occur between the following limits:

	%		%
α-Pinene ..	7-10	Linalol ..	17-24
d-Limonene	38-46	Linalyl acetate	22-32

The composition of Florida cold-pressed murcott oil has likewise been examined using similar analytical techniques.[5] The oil from this fruit (also known as the Smith tangerine or Murcott honey orange) has a similar flavour, i.r. characteristics and the same chemical components as Dancy tangerine oil. However, the constituents are present in different proportions. Tangeretin was also isolated and identified in murcott oil. Other properties reported were: d_{25}^{25} 0·8441-0·8442; n_D^{20} 1·4737; α_D^{25} +96·48; aldehyde, 1·09-1·26%.

Lavender oil

Continuing his studies on the minor components of French lavender oil, Naves now states[6] that the presence of α-ocimene reported previously[7] is incorrect. However, β-ocimene has been definitely established together with α-pinene (0·01%), camphene (0·02%) and 0·01% of sabinene and (+)-nopinene.

Geranium oil

The substituted tetrahydropyran, (+)-epoxydihydrolinalol, which was recently reported as occurring in French lavender oil to the extent of 0·02% (MANUFACTURING CHEMIST, Feb., 1961), has now been isolated from Bourbon geranium oil in 0·34% yield.[30] This material appears, during distillation, just prior to linalol together with *cis*- and *trans*-dehydrocitronellol. The latter compounds were shown to be 2(2-methylpropenyl)-4-methyl-tetrahydropyrans,[31] having a structure similar to the oxides of Seidel and Stoll isolated from rose oil. The characteristics reported were:

cis-dehydrocitronellol (0·68% yield), α_D-15·30; d_4^{20} 0·8659; n_D^{20} 1·45650
trans-dehydrocitronellol (0·33% yield), α_D-18·0; d_4^{20} 0·8867; n_D^{20} 1·45815

Buchu leaf oil

Continued interest in the composition of natural products primarily used for flavouring is shown by a recent publication,[8] which describes the isolation of 90% of *l*-pulegone from *Barosma crenulata*, and somewhat smaller amounts from *B. betulina*. The authors claim this to be the first report of the isolation of this material (α_D^{20} —19·5; semicarbazone, m.p. 171°C.) from natural sources. *B. betulina*, the well-known buchu oil of flavouring, also contains appreciable amounts of diosphenol (buchu camphor). The latter has now been found to be a two-component mixture. Approximately 45% consists of ψ-diosphenol (m.p. 38°C.), an isomer with similar i.r. spectrum to diosphenol (m.p. 83°C.), which spontaneously reverts to the latter compound. A method is also proposed for estimating the total diosphenol in buchu oil. This depends on measurements (in ethanol) of corrected u.v. absorbance at 272 mμ and applying the relationship:

$$\%\ (W/W)\ \text{Total diosphenol} = \frac{E_{corr} \times 100}{W \times 391}$$

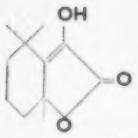
where W is the weight of sample (g.) per 100 ml. of solution.

Bitter carrot oil

Steam distillation of canned bitter carrots followed by ether extraction of the distillate gives 0·0025% of an essential oil.[9] Fractionation of this oil yields approximately 40% of a liquid $C_{14}H_{18}O_2$ (b.p. 108°C./3 mm., n_{20}^{20} 1·5074; d_{20}^{20} 0·9628; $[\alpha]_D^{20}$ + 5·14) having the typical flavour of carrot root. The compound shows a characteristic u.v. absorption at 280 mμ and is considered to be quite different from carotol, a component of carrot seed oil.

β-cyclocitral

Among the publications relating to aromatic chemicals is a novel preparation of β-cyclocitral from β-ionone.[10] Tiemann oxidation of the latter with permanganate in acetone followed by pyrolysis of the product under nitrogen gave 63% yield of β-cyclocitral. The intermediate compound, which is a solid γ-lactone subliming at 129°-131°C., was shown to have the following constitution:



As may be seen, this is not unrelated to several known perfume and flavour aromatics which have a similar C—C—C(OH)—CO— ring structure. However, no odour characteristics of this compound were reported.

Aromatic chemicals from pinene

A number of British and American patents have recently been granted covering the manufacture of a wide range of terpenoid compounds from pinene and its derivatives. A British patent[11] describes the pyrolysis of 1,8-*p*-menthadien-3-ol or *trans*-isopiperitenol, obtained from verbenol,[12] at 390-415°C. to give a mixture of citral and isocitral. Approximately 45% conversion is achieved with 13% loss, the unchanged menthadienol being recycled after careful fractionation of the product. The normal synthesis of citronellol from β-pinene involves the production of myrcene by thermal cracking followed by selective hydrolysis of myrene hydrochloride. A new route employs citronellene (2,6-dimethyl-2,7-octadiene) as starting material.[13] This material, which is readily obtained from the pyrolysis of pinene, reacts with aluminium hydride in ether to give the corresponding trialkyl aluminium complex. This is finally hydrolysed in the presence of air to give citronellol. Catalytic hydrogenation of hydrochlorinated verbenone yields a very useful mixture of products.[14] These include *p*-menthone and *iso*menthone (25%) and *cis-o*-menthone (10%). This forms a useful alternative route for the production of synthetic menthol from turpentine. Pyrolysis of verbanone at 350°-700°C. gives up to 22% of *cis*-o-menthen-3-one (b.p. 95°-98°C./10 mm), a new compound with a spicy, minty odour and recommended for use in perfumes and flavours.[15] Finally, limonene oxide (obtained by peracid or air oxidation of *d*-limonene) has been pyrolysed under pressure at 300°C. to a mixture of dihydrocarvone, *l*-carvone, *l-cis*-carveol and *d-cis*-pseudocarveol.[16] Oppenauer or chromic acid oxidation readily converts the latter compound to *l*-carvone.

The commercial synthesis of linalol and the rose alcohols via myrcene and nerolidol or linalol from acetylene is well known. These products are now firmly established on the market. The improved and hitherto unknown odour characteristics of these pure aromatics present new possibilities for the perfumer's creative ability.[17] Nerol, citronellol and linalol can be used in much higher proportions without unbalancing a perfume formulation. This is due principally to the absence of undesirable terpene and sesquiterpene impurities. Attention is drawn to pure nerol in particular because of its unique odour qualities which give a touch of natural freshness to floral compositions. The following is recommended for a lily-of-the-valley composition using over 70% synthetic terpene aromatics:

Syringa aldehyde 50%	5
Methyl anthranilate 10%	10
Civet natural 10%	20
Benzyl acetate	20
Amylcinnamic aldehyde	20
Citral	10
Linalyl acetate	20
Petitgrain oil (Fr.)	30
Phenylethyl alcohol	50
Anisyl alcohol	100
Nerolidol	100
Linalol	100
Citronellol	100
Hydroxycitronellal	200
Nerol	215
	1,000

Solubilities of essential oils and aromatics

An attempt has been made to apply systematically the H.L.B. system (Hydrophile - Lipophile Balance) of Griffin[18] to the aqueous solubilisation of lavender and lime oils.[19] Oil/emulsifier ratios of 1·0 produced clear solubilisation, especially when applied to a mixture of an anionic sulphated ethoxylated alkyl phenol with a non-ionic ethoxylated alkyl phenol. H.L.B. values for solubilisation of essential oils generally lie between 13 and 17, each oil having a very narrow range in which solution is complete. Thus, lavender oil showed values of 13·8-13·9 while lime oil gave 13·7-13·8. Some materials, such as methyl salicylate, were not easily categorised, probably owing to the formation of complexes with some emulsifiers.

In a 16-month test on the solubilities of some 30 common essential oils and aromatic chemicals in aerosol propellants,[10] lavandin oil and coumarin were insoluble at 1%

in propellant 114 and in a 50/50 mixture of propellants 11 and 12. Complete solubility in both propellants was shown by *Abies sibirica*, almond, cedarwood, lemongrass and peppermint oils, amyl butyrate, geraniol, methyl benzoate, musk ambrette and styrallyl acetate.

Perfume fixatives

Theories relating the persistence of perfume components to their volatility continue to receive close attention. A recent paper by F. V. Wells[21] gives the boiling points and volatilities of over 200 aromatic chemicals in descending order. Another paper[22] reports the effect of several musk compounds on the evaporation time (on a blotter) of benzyl acetate and methyl amyl ketone. Recently, Jellinek published a very useful systematic theoretical and practical study of the evaporation process[23] as an extension of previous work. By recording the gas chromatograms of the actual vapours above certain three-component mixtures, the relative peak heights were used as a measure of individual odour intensities. Results indicated that high-boiling components (present at concentrations >40%) selectively reduce the evaporation rate of odorants of similar structure. For example, the peak height ratio of *n*-heptyl alcohol to benzyl acetate was reduced from 2·8 to 2·1 by the addition of linalol. Similarly, in a linalol/ethyl benzoate mixture, diethyl phthalate and nerolidol reduced the vapour pressures (*i.e.* relative peak heights) of ethyl benzoate and linalol respectively. Using the same experimental technique, the author also confirmed previous observations by smell of the effect of water and mineral oil as solvents on the vapour pressure of a 50/50 linalol/phenylethyl alcohol mixture. Thus, a 0·5% solution of the mixture in oil increased the original peak height ratio (of the concentrate) from 2·0 to 5·8, but in water it was increased further to a point where the phenylethyl alcohol peak was negligible. It was concluded that: (*a*) the molecular attractive forces of an odorant with the surrounding fixative molecules affects the odour intensity; (*b*) the magnitude of these forces depends on the relative structural relationship of the molecules.

The above line of thought has been independently supported, in part, by a Russian author who discusses the problem from the theoretical viewpoint.[24] However, he considers that the persistence of a perfume as a whole is not *entirely* dependent on its evaporation rate. Traces of animal constituents such as musk, civet, etc., probably act physiologically in reducing the threshold concentration of the other perfume ingredients. By means of odour energy values (given by $E = 1/k \times 720$—where k is the threshold concentration) he attempts to rationalise the factors responsible for compounding a persistent perfume.

Analysis of natural products

For successful analysis of complex mixtures such as essential oils or fruit aromas by gas chromatography, a preliminary separation into functional groups is necessary. A new method for the quantitative recovery of small amounts of steam volatile C_2-C_5 fatty acids from aqueous solution has been described.[25] The solution of fatty acid sodium salts is evaporated to dryness and cold treated with 30% sulphuric acid. The mixture is then passed through a column of Celite 545 packed over anhydrous calcium sulphate, and washed with dry ether. After removal of solvent (6 mm press. and −50°C.) the pure acids are finally separated on a silicone/stearic acid GLC column at 137°C. Apart from formic acid, which gave low values, nearly theoretical results were obtained for all the acids tested. This method should prove particularly useful for the identification and estimation of free or combined acids in natural fruit aromas.

In the direct GLC analysis of essential oils, the separation of polar constituents can be complicated by tailing of the peaks, especially with non-polar stationary phases such as silicone grease. Peak definition and symmetry is improved by the addition of 10% lithium caproate.[26] By combining this technique with the selective chemical separation of compounds having the same retention time, 15 components have been separated from Bourbon geranium oil, including fenchyl alcohol and menthone.

Aldehydes

The detection and separation of traces of certain aldehydes may be accomplished by the selective hydrolysis of their dimedone derivatives.[27] In contrast to other aldehydes, the dimedones of formaldehyde, $\alpha\beta$-unsaturated aldehydes and *o*-hydroxyaldehydes do not hydrolyse under weakly alkaline conditions (*p*H 8-9·5). The unreacted derivative can therefore be filtered off and the aldehyde subsequently regenerated in acid solution.

Apart from dimedone, there is not a very wide variety of specific reagents for characterising aldehydes. A new compound (*dl*-1,2-dianilino-1,2-diphenylethane) has now been reported.[28] This reagent, which is prepared by reductive condensation of N-benzylidene aniline, reacts readily and specifically with aliphatic aldehydes and substituted benzaldehydes to form good yields of crystalline imidazolidines.[29] These compounds have sharp melting points over a very wide temperature range. The test aldehyde is simply added to a 1 : 1 acetic acid : acetone solution of the reagent, reaction being complete after a few minutes. Furthermore, molecular weights of derivatives can be quantitatively determined by potentiometric titration in acetic anhydride with 0·1 N perchloric acid in glacial acetic acid. The accuracy of analysis is generally better than 1%. Some examples of melting points are given below.

Aldehyde derivative	m.p. °C.
Acetaldehyde	160-161
C8	150-151
C9	118-119
C10	88-89
C11	70-71
C12	68-69
Cinnamaldehyde	214-215
Hydrocinnamaldehyde	205-207
Phenylacetaldehyde	155-156

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FERTILISERS and Plant Nutrients

By D. P. Hopkins, B.SC., F.R.I.C.

Rothamsted report • Nitrogen and grass • Urea • Fixation of nitrogen by legumes • Protective coatings for fertilisers • Responses of crops • Sodium as a nutrient • Manufacturing innovations • Fertiliser use in Europe Losses of nitrogen from urea

Manures and organic matter

THE new Rothamsted Report[1] reveals that the current approach at Rothamsted is to try to separate the physical and nutrient-providing effects of manures and organic matter. Though this view has been criticised, Rothamsted firmly adheres to the conclusion, based upon many long-term and continuous tests, that on soils of the somewhat heavy type (as used at Rothamsted) there is no evidence that farmyard manure provides benefits other than those due to its content of essential nutrients. On very light soils, as at Woburn, some comparative experiments have shown that FYM gives better yields than fertiliser dressings, but the variations in FYM composition make it difficult for non-elaborate experiments to be precisely comparative. For some crops there may too be a placement advantage for the nutrients given in FYM, which is usually ploughed under, whereas fertiliser dressings are applied to the top 3 in. of the soil; for crops which go through main development stages in the summer and later summer period, the nutrients in FYM may well be in moister soil and therefore more active. Even on the poor-structured Woburn soil, arable yields after 30 years of six-course rotation are higher now than at the start of the experiment on plots where only mineral fertilisers have been used. On such soils, organic matter may be necessary but it need not be given as FYM. Organic matter residues from periods under ley can be fully effective.

Thin sections of soils have been studied for stability and permeability. Continuous grass had more beneficial influence upon these physical qualities than annual applications of FYM. This new method of testing soils for their structural condition is being developed at Rothamsted, but it will need wider application to many more soils before it can be reliably employed in advisory work for farmers.

Nitrogen

The effect of different N fertilisers upon the *type* of nitrogen in grass has been compared. Nitrate fertilisers gave definitely higher nitrate-N contents in ryegrass, whereas ammonium sulphate gave higher amide-N and amino-N contents. Even one month after application, by which time the nitrate-N contents of all grasses had dropped, nitrate-N in grass fed with nitrate fertilisers remained higher than in grass fed with ammonium sulphate. This confirms previous results. It could have important consequences when at present nitrate type fertilisers are increasingly available as "straights" and when nitrogen use on grassland is becoming steadily more intensive; for other work has indicated that high contents of nitrate-N in grass can be metabolically undesirable.

Urea

The efficiency of urea as concentrated N fertiliser has been closely investigated. It may contain biuret as a degradation impurity and biuret can be toxic. It forms ammonium carbonate or bicarbonate when it decomposes rapidly in soils and this can produce a high *p*H close to seedlings and also a high NH_3 concentration—in addition N may be lost by NH_3 volatilisation. Tests have measured the N losses and it would seem that the least loss of this kind occurs with heavy soils; also, that the risk of loss may be reduced if the urea is worked into the top inch of soil and not merely broadcast on the soil surface. The effect of biuret is shown by these germination percentages (kale seed) when different ureas were used at two rates:

	% Biuret	*% germination*
Granular urea	(6) ..	.. 56
Prilled urea	(1·5) ..	.. 85
Crystalline urea	(0·6) ..	.. 71
Pelleted urea	(0·5) ..	.. 82

Another Rothamsted contribution on urea has recently been published in summarised version,[2] and in the discussion on this paper it was pointed out that when urea is granulated as a constituent of NPK mixtures the formation of biuret during the heated stage of the process is repressed by the presence of water-soluble phosphate. As urea seems most likely at present to be developed in this country as a part-source of nitrogen for mixed fertilisers, it would seem that studies of its fertiliser properties and behaviour should be related to these conditions of processing and use.

The effectiveness of the magnesium content of basic slag has been investigated, and small-scale tests with ryegrass showed that "part at least" of the Mg in slags is available to grass. Open-hearth slags contain more Mg (about 5 to 6%) than Bessemer slags (about 1%); a 5 to 10 cwt. per acre dressing of the former type of slag would provide 25 to 40 lb. of Mg. Even partial uptake of this amount of magnesium must be valuable on soils low in this nutrient.

N fixation by legumes

A U.S. paper[3] describes the interactions between fixation of N by beans and supplies of mineral nutrients. With inoculated bean plants, fixation (and growth and yields) was much increased if P, K, Ca and Mg were liberally provided. However, these effects were most marked when moderate amounts of inorganic N were also given—an observation that runs counter to the older view that leguminous fixation of N may be repressed if nitrogen is given in other forms. With bean plants that were not effectively inoculated, however, the amount of N fixed by the plants could not be raised by the provision of other nutrients.

Coatings for fertilisers?

Coating fertilisers with surface protectant materials has been advocated for conditioning reasons, but a new U.S. paper[4] examines this as a concept for protecting nutrients

from leaching losses. Most fertiliser in America, as here, is applied before crop sowing or at the time of sowing. As the needs of very young plants are small, the soluble nutrients in fertilisers may be partly lost or moved out of reach before the larger and later needs of the crop have to be met. (It might be said at this point, however, that this question of possible loss is one of supposition, and it would be more valid to measure such losses first before considering remedies for them. In fact, some soluble nutrients are loosely fixed by soil components and kept available to crops—this occurs instead of loss by leaching.)

Various fertilisers were coated with vinyl acetate, acrylic resin, paraffin and a polyethylene emulsion—in general, granular fertilisers were used. The beneficial results obtained were of three kinds. First, seed germination under contact conditions was better with coated than with uncoated fertiliser. Second, coatings reduced leaching losses with potassium—but this was shown only by laboratory experiments imitating the effects of leaching, and it would appear that the fertilisers themselves were leached, *not* fertilisers mixed with any soil. Third, lucerne in a field experiment when dressed with a coated 5—20—20 granular fertiliser took up less " luxury " potash than lucerne dressed with a similar but uncoated fertiliser. Drawing practical conclusions about the first and third of these findings would seem more valid than doing so about the second.

It is mentioned in the paper that applying coatings to fertilisers is much simpler with well-rounded granules than with angular and irregularly-shaped granules. With the former a coating will amount to only about 1 to 5% of the fertiliser's uncoated weight. With the latter, rounding the granules by tumbling them with an inert material and binding agent may be necessary before coating, in which event the additional weight due to coating must be considerably higher.

Fertiliser responses

Dr. Boyd has this year published two papers[5,6] which re-examine and re-discuss the subject of response curves for yield-fertiliser relationships. It is clear that much of the pre-1940 testing, on which the Crowther-Yates concepts were based, was done with fertiliser rates that were low by today's standards. Broadly, the Crowther-Yates thesis provides a response curve that rises rapidly and gradually flattens out, *i.e.* eventually applying extra fertiliser merely keeps the yield at a maximum. This concept of an exponential form of response curve is not supported by post-1940 test data for various crops. Rather, the response curve rises to a maximum and then begins to fall, *i.e.* extra nutrient supply after the maximum yield point will reduce yields. Also, the point when the yield-fall begins depends for any single nutrient upon the amounts of nutrient already in the soil and upon the level at which other nutrients are present either naturally or as added materials. Dr. Boyd's revised view of response curves must make advisory work much less simple than when based upon the former—and still largely current—concept of exponential curves. However, rates of fertiliser for optimum yields are usually slightly below the rates for maximum yields, and therefore much farm practice with fertilisers would be plotted on the first portion of either kind of responsive curve—and this first portion is similar in shape, whether exponential or parabolic. The problem of anomalous results seems most likely to arise when soils contain larger N, P or K reserves than is supposed—in such cases optimum or near-optimum rates will in fact create conditions that would be plotted on the second part of the curve, which on the Boyd thesis would mean lowered yields, on the Crowther-Yates thesis static yields. To make this point is not to reduce the practical significance of Dr. Boyd's contributions. At any rate for major arable crops, this significance becomes larger as more and more fertiliser practice becomes intensive and optimal. After some years of optimal dressings, the question of the value of residues of the dressings becomes highly important, for these reserves could put the effect of further dressings into the descending part of the Boyd parabolic curve. The principal significance of this work is that it draws attention to the urgent need to have better methods for evaluating nutrient reserves in soils.

Sodium

A new paper has proved, if further proof were needed, that sodium is a direct nutrient for sugar beet.[7] In fact the paper is based upon results of the 1940s which were not then published by the late Dr. J. B. Hale. Plants were removed during two seasons of salt and potash trials; analysis of the plants showed that although salt raised crop yields it did not raise potash uptake nor did it in any way stimulate extra mobilisation of soil K reserves. An interesting finding was the differing distribution of K and Na in the beets at harvesting—6% of the plant's total Na could be found in the root, but 33% of total K was in the root.

Another British paper[8] has investigated the use of salt on grassland, a treatment long practised in salt-mining areas, *e.g.* Cheshire. No yield responses to salt applications could be measured on small plots one year old, and in one case clover in a mixed sowing was badly scorched by the salt. At the same time, it must be mentioned that potash fertilisers also gave no yield responses. To check whether salt would give a response as the soil's potash reserve was used, one plot was continued for three years, but salt still failed to increase output.

Fertiliser manufacture

The use of wet-process phosphoric acid in making high-analysis liquid fertilisers has been handicapped by precipitation due to impurities. A TVA study[9] has shown that this can be eliminated by sequestering the impurities by adding superphosphoric acid or ammoniated superphosphoric acid, the sequestering effect being due to pyrophosphates or polyphosphates. If the liquid NPK fertilisers are to be safely stored without precipitation troubles, 30 to 40% of the final P_2O_5 content should be derived from the added superphosphoric acid.

Attempts to relate fertiliser efficiency with size of granules have not been numerous. Another U.S. investigation[10] has tested various sized granules made from a range of laboratory-prepared water-insoluble phosphates. These phosphatic materials had from 23 to 99% of their P_2O_5 contents in the citrate-soluble form. In general, the finest-sized granules were the most effective for the test crop, corn. As the granule sizes rose, efficiency increasingly depended upon the amount of citrate-soluble P_2O_5 in the fertiliser material. This trend was not as definitely displayed by the smaller-sized granular materials. There is in this work an indication, though hardly proof, that readiness of phosphate solubility can be a more

influential factor for efficiency than differences in granule sizes.

Some new slowly-acting phosphatic materials have been reported.[11] These are a magnesium ammonium phosphate testing 8—40—0 and a ferrous ammonium phosphate, 7—35—0. The former's Mg content is 24% as MgO. The phosphate is of low solubility, but it becomes slowly available as the compounds decompose—the nitrogen becomes available by dissolution and also by nitrification. Long duration for the P and K supply and freedom from possible scorch damage are claimed to make these new fertiliser materials suitable for forestry seed-raising.

European fertilisers

The 10th trade study for fertilisers in O.E.E.C. countries, covering 1958-61, has been published.[12] It deals particularly with 1959-60 data and estimates for 1960-61. 1959-60 production again showed an increase, 6% for N, 6% for P and 7% for K. For P and K this is a larger rate of expansion, for N a slightly smaller one. Consumption for the same period also rose by 7, 4 and 4% for N, P and K. An important change was a 24% rise in exports of N fertilisers to non-O.E.E.C. countries; this follows an export decline in 1958-59. Among specific fertilisers, urea production expanded in 1959-60 by 35% as against a 21% expansion in the previous year. Ammonium nitrate production, after not expanding recently, rose again by 10%. Nevertheless, urea still represents much under 2% of total N fertiliser consumption. The use of sulphate of ammonia declined by 9%, that of ammonium nitrate increased by 13%. Prices in 1959-60 for all fertilisers were kept stable in most O.E.E.C. countries.

Losses from urea

An American paper[13] received just as this report was completed substantially confirms Rothamsted evidence mentioned above about losses of gaseous ammonia from surface-applied urea. Nitrogen losses of this nature were 29% on unlimed turf, 39% on limed turf. By comparison, losses with sulphate of ammonia were 0·4 and 19·7%, with ammonium nitrate 0·3% and 3·4%. With urea applied to bare light soil there was a 25% loss in seven days. Somewhat unexpectedly, losses were greater from granules of urea than from finely particled urea; this could be due to greater soil absorption of the finer material. Dusting the urea with gypsum and with copper sulphate was tried, but it did not reduce the losses. It seems clear that surface applications of urea should be avoided for light soils or turf and, if possible, the urea dressing should be worked into the top soil.

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Extrapones. The properties and uses of these cosmetic materials are described in "The Extrapone Vade Mecum" issued by Dragoco Holzminden. Thirty-eight formulæ are given.

Pharmaceutical Formulation Problems

*The investigation of dispensing and formulation problems submitted by members is an important part of the work of the Department of Pharmaceutical Sciences of the Pharmaceutical Society of Great Britain. From the Department's latest report come the following examples of problems investigated and the results obtained.**

Sulphonamide mixtures for infants

THE reformulation of mixture of succinylsulphathiazole for infants and mixture of sulphadimidine for infants using methylcellulose derivatives as suspending agents was examined. Suspensions prepared with various grades of methylcellulose sedimented more slowly than suspensions containing compound powder of tragacanth, but considerable frothing occurred during preparation and on shaking the bottle. Suspensions prepared with sodium carboxymethylcellulose (medium-viscosity grade) were more satisfactory; sodium carboxymethylcellulose was much easier to disperse in water and it also caused far less frothing. It was recommended that 0·5% of sodium carboxymethylcellulose be used for mixture of succinylsulphathiazole for infants, and 1% for mixture of sulphadimidine for infants.

Ichthammol in creams and ointments

Following a recent report that there is considerable variation in the pharmaceutical properties of ichthammol complying with the B.P. specifications, two samples of ichthammol were bought from different commercial sources. Although both samples gave similar analytical results when examined by the B.P. tests and assays, differences in pharmaceutical properties were observed. For example, 2% of one sample in cream of zinc oxide gave rise to gross separation within seven days, whereas the other sample produced a stable homogeneous cream. In cream of calamine, the addition of 1% of one sample resulted in immediate separation, whereas the other sample produced a cream in which slight separation occurred only after several weeks.

Ointment containing phenol—instability

An ointment made to the following formula became extremely gritty on keeping and could not be used in the treatment of eczema, for which it had been prescribed:

Liquefied phenol 2 minims, strong solution of lead subacetate 10 minims, zinc oxide 90 grains, glycerin 90 minims, white soft paraffin to 480 grains.

Possible causes were: (1) separation of phenol—it is advisable to use phenol crystals rather than liquefied phenol; (2) phenol solutions react with lead subacetate solution to produce an oily precipitate which is, however, soluble in glycerin. In the laboratory the following method was adopted: dissolve the liquefied phenol or the equivalent amount of phenol crystals (2½ grains) in the glycerin and triturate with the zinc oxide (in fine powder) to form a stiff, smooth paste; mix with the white soft paraffin and finally incorporate the lead subacetate solution. An ointment prepared in this way has remained stable for four months.

Alternatively, it was suggested that wool fat (5%) or white beeswax (5%) be incorporated as a stabilising agent. Ointments prepared with these materials have also remained stable; the consistency is, however, different from that of the original ointment.

Ointment containing potassium iodide

Advice was sought on dispensing an ointment containing 20% of potassium iodide in wool fat, in which a brown colour had rapidly developed. This was confirmed, the colour developing within a few hours. The following formulæ were tried:

(1) Potassium iodide 20 g., sodium carbonate 0·5 g., water 25 ml., anhydrous wool fat to 100 g., and (2) potassium iodide 20 g., sodium thiosulphate 0·2 g., water 25 ml., anhydrous wool fat to 100 g.

Both preparations remained pale yellow for several weeks, although very slight discoloration occurred on the surface of that made according to formula 1. Exposure to light appeared to accelerate discoloration. It was advised that, preferably, small amounts should be dispensed (*e.g.* one week's supply) at a time and packed in well-filled containers, protected from light.

Mixtures containing tincture of belladonna

Some, but not all, batches of tincture of belladonna sometimes give rise to a greenish deposit or scum of colouring matter when diluted in mixtures, *e.g.* in mixture of belladonna and ipecacuanha for infants. The laboratory has found that the addition of tincture of quillaia (2½ minims per fl. oz.) aids dispersal of the deposit or scum. Alternatively, the addition of 1% of cetomacrogol 1000 may give a clear solution. Cetomacrogol should not be used if there is a high concentration of electrolytes present, since the cetomacrogol may be "salted out."

HCN in syrup of wild cherry

Four commercial samples of syrup of wild cherry were assayed for hydrogen cyanide; no HCN was detected in any sample. A sample of wild cherry bark was assayed and was found to yield 0·096% w/w of HCN. This sample was used to prepare 200 ml. of syrup of wild cherry. The resulting syrup was assayed immediately after preparation and was found to contain 0·0058% w/v of HCN; the loss of HCN during preparation of the syrup was 59%. This syrup is being stored for later examination.

The following assay method was used: to 25 ml. of wild cherry syrup add 5 ml. of dilute sulphuric acid; add a small piece of marble and steam-distil into 20 ml. of N/100 sodium hydroxide. To the distillate add 5 ml. of 20% phosphoric acid and sufficient bromine water to produce a persistent yellow colour, allow to stand for 5 min. and decolorise with 2 ml. of a 5% w/v

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solution of phenol. Add 0·5 g. of potassium iodide, allow to stand for 5 min., and titrate with N/50 sodium thiosulphate using starch mucilage as indicator. Each ml. of N/50 sodium thiosulphate is equivalent to 0·0002702 g. of HCN.

Cream containing iodine—formulation

Advice was sought on a suitable basis for a cream containing in each 2 oz., iodine 8 grains, menthol 17 grains, strong tincture of capsicum 2 minims, camphor 34 grains, and methyl salicylate 34 minims. The enquirer had tried several bases but gross separation had always occurred on standing. A smooth homogeneous cream was prepared using, as the basis, cetomacrogol emulsifying ointment 1½ oz. and water to 2 oz.; potassium iodide 8 grains was added in order to dissolve the iodine in the aqueous phase. The following method of preparation was recommended: mix the camphor and menthol to form a semi-solid mixture and add the methyl salicylate and strong capsicum tincture; add this oily solution, in small portions at a time, to the cetomacrogol emulsifying ointment and rub down until homogeneous; dissolve the iodine in a solution of the potassium iodide in the water, and gradually incorporate this solution in the cream. No separation occurred during three months' storage.

Non-ionic surfactants. Croda Ltd. have published another technical data sheet describing *Polychol* non-ionic surfactants, a range of polyoxyethylene derivatives of lanolin alcohols. The 8-page booklet gives details of composition and properties, function, manipulation, uses and handling and storage requirements. A similar publication describes *Crodex* and *Cerawax* emulsifying waxes.

Heat transfer medium. A brochure describing I.C.I.'s new heat transfer medium *Thermex* lists physical and physiological properties, composition data, uses and suggested uses and packages for the product, together with tables and graphs. *Thermex* is I.C.I.'s adtremark for a eutectic mixture of diphenyl oxide and diphenyl which is suitable for application as a heat transfer medium at temperatures up to 400°C.

Anti-Schistosome Drugs—M.R.C. Research

It has been estimated that at least 80 to 100 million people are infected with the bilharzia blood flukes, or schistosomes; the increase in prevalence, and to some extent in severity, of bilharzia disease is a grave menace to public health. There are three species of human schistosomes: *Schistosoma hæmatobium*, which is found in the Middle East and Africa, affects the urinary tract, while *S. mansoni*, found in Africa and Central and South America, and *S. japonicum*, found in the Far East, damage the intestine. Each form may also damage other organs, especially the liver. The flukes live in the blood vessels and discharge large numbers of irritant eggs; these ulcerate their way through the tissues into the intestine or bladder and hatch when the host's excreta fall into water. The larvæ then enter water snails and multiply greatly, giving rise to numerous infected larvæ; these may penetrate human skin when people go into infected water. In man the larvæ grow into adult flukes in two or three months.

A curative drug can act in three ways: (1) directly, with a lethal action on the flukes, (2) indirectly, with a similar action after it has become altered or broken down in the body, or (3) by a mechanism not yet well understood which raises the efficiency of the host's defences.

Antimony appears to act directly on one stage of the parasite's sugar catabolism, but it probably has other actions since it can cause great overactivity of some schistosome species *in vitro*. The thioxanthone—lucanthone, or Miracil D—which has been in use for ten years, does not seem to act directly on the flukes; it troubles them little when added to serum medium *in vitro*, but the serum and blood of treated patients is damaging to the parasite.

The Medical Research Council's Bilharzia Research Unit at St. Albans, Herts., has improved the method for estimating lucanthone, and is investigating the metabolites produced in urine and blood. Lucanthone is given by mouth as the hydrochloride and is very unpleasant to take. Recently the Unit has had some success in preventing the side effects by the use of preparations in which the drug is attached to resins. These resinates reduce the rate of absorption of the drug from the intestine to the minimum necessary to provide a curative concentration in the blood, and they are being used to treat patients too ill to receive antimony.

Lucanthone resinate has a further advantage over the hydrochloride; more drug can safely be given in less time, the standard course at present being three or five doses in 48 hr.

The diphenoxyalkane group of compounds stimulates defence mechanisms in rodents, but has not yet proved suitable for use in man, probably because of a species difference, since one of the most likely of these compounds was found by the Unit to be inactive in baboons. In mice it rapidly removed all flukes; they were found in the liver, often still moving but heavily sheathed and coated with white blood cells—literally eaten alive.

Some drugs need only paralyse the flukes partially, their action in setting the defensive cells to work providing the *coup de grâce*. Recent work at the Unit suggests that the degree of this phagocytic response may be related to the immunity of the host. In time it should be possible to put anti-schistosome drugs through a series of *in vitro* tests to show whether they act directly, or indirectly through metabolites or host defence mechanisms. Knowledge of their mechanism of action can then form the basis for rational attempts to alter them chemically to make other more effective compounds.—*From the Report of the Medical Research Council*, 1959-60.

Drugs in the Treatment of Disease

British Medical Association, London. 1961. *Pp.* x+516. 35*s. net.*

THERAPEUTICS, although once almost entirely an art, is still far from being an exact science. Yet the advances in recent years in the understanding of many physiological processes, and the relationships between chemical structure and pharmacological activity, have virtually transformed the drug treatment of disease, and are now no longer merely symptomatic, but can be directed at the cause.

These advances, however, like troubles, come " not in single spies, but in battalions " and often bring problems with them. Newer remedies tend to appear in groups, each member of which has a well-defined basic action, but with individual variations in potency, dose and other properties. The busy practitioner has difficulty in assessing the relative value of such drugs, but in this book experts in various branches of medicine offer valuable guidance through the increasingly complex maze of modern remedies.

The book consists of a series of articles which appeared in the *British Medical Journal* from 1958-60, and since revised and grouped into 13 sections. Representative sections are exemplified by those on sedatives, hypnotics, analgesics and anti-histamines; the cardiovascular system; the nervous system; anæmia; skin; special sense organs; and general.

The chapter on corticosteroids and analgesics in rheumatoid conditions warns that the former affect the patient as a whole, not merely his painful joints, and are but supplementary to the main form of treatment, which is rest. This practical aspect is evident in most parts of the book, but as is almost inevitable in a collection of articles of this kind, there is some unevenness of approach by different authors. Thus the new benzothiadiazine diuretics are adequately reviewed in the chapter on diuretics, but only one receives mention in the chapter on chronic heart failure. In a book designed to aid the busy prescriber, structural chemical formulæ should be few and representative, and it seems unnecessary to have 17 graphic formulæ of androgenic compounds. The brand names of available anabolic steroids with reduced virilising effects could have been given.

The concluding section of the work, headed " general," has chapters on pædiatric prescribing; prescribing for old people; the control of the sale of poisons; drug addiction; and the treatment of poisoning. These chapters on prescribing bring together much information not usually readily available, and in this age of synthetic drugs it is refreshing to find that the value of tincture of belladonna as an antispasmodic has not been forgotten.

The book offers practical guidance on the use of drugs. It will be of material help to the discriminating physician and a useful " refresher " for all interested in modern therapeutics.

S. J. HOPKINS.

Synthetic Ion-Exchangers

By G. H. Osborn. 2nd Edn. Chapman and Hall, London. 1961. *Pp.* 346. 50*s. net.*

IT is barely six years since the previous edition of this book, proof enough of the rapid progress of ion-exchange. The author has wide experience of the subject and he uses it to critically review the latest knowledge and developments in theory and practice. He has cut out involved theory and used the space saved for a description of newer and more practical aspects of ion-exchangers. New subjects include ion-exchange for effluent treatment, for large-scale production of deionised water and for catalysts and the jigged-bed or pulsed technique. Some 500 titles have been added to the excellent classified bibliography which takes nearly 200 pages.

Gas Chromatography Abstracts

Sponsored by the Gas Chromatography Discussion Group. Edited by C. E. H. Knapman and C. G. Scott. Butterworths, London. Pp. 200. 42*s. net.*

LIKE every other fashionable subject gas chromatography inspires more and more papers. So it is not surprising that this book contains 158 more abstracts than the last—875 to be exact. There are author and subject indexes and the promise of a cumulative index in 1963 to cover the 1958-1962 volumes.

The widening interest in the subject guarantees an increased readership. It might be bigger if a less expensive paper and binding were used enabling the book to sell at, say, 25*s*. Is it really necessary to have board covers hefty enough for a bible?

New and Nonofficial Drugs 1961

Lippincott, Philadelphia. 1961. *Pp.* 849.

THIS annual compilation is as useful as ever. As the name implies it covers drugs generally available in the U.S. that have not become official by entry in the U.S. Pharmacopœia or the National Formulary. Information is classified pharmacologically, the first chapter covers anæsthetics and the penultimate one vitamins; the last is " Miscellaneous." The individual monographs give the therapeutic, prophylactic and diagnostic status of the drugs as evaluated by the council on drugs of the American Medical Association. The book is indispensable for keeping completely informed of drug developments in the U.S.A.

Principles of Chemical Equilibrium

By P. G. Ashmore. Royal Institute of Chemistry, London. 1961. *Pp.* 49. 4*s.* 6*d. net.*

THIS is the fifth R.I.C. Monograph for Teachers, a series of dissertations on well-defined topics in chemistry for the guidance of teachers at the advanced level of the General Certificate of Education. It is in three parts: energy changes and conditions for equilibrium; chemical equilibrium in ideal and real systems; and the determination of equilibrium constants.

▶SWISS SPRAY DRYERS TO BE MADE IN U.K.

Steel and Co. Ltd., Sunderland, has taken over the technical and commercial assets of the spray dryer business of Luwa A.G. of Zurich, Switzerland, and will manufacture Luwa spray dryers in the U.K.

Design, manufacture and installation of Luwa spray dryers will be carried out by Steels Process Plants Ltd., Eastcote, a subsidiary company of Steel and Co. Swiss engineers will assist the staff of Steels Process Plants in the U.K. and Steel's engineers have already undergone training at Luwa's Zurich factory.

Two test plants—one a spinning disc tower and the other a combined high-pressure nozzle and spinning disc tower—are being installed at a research and test laboratory in the Sunderland factory of the Steel Group. The plant, which is equipped with both the spinning disc and pressure nozzle methods of atomisation and arranged alternatively for co-flow and counter-flow of air, permits full-scale industrial tests, easy comparisons, the evolution of new drying techniques and the development of new products. On this latter point the company state that, appreciating the need for absolute secrecy which often surrounds new developments in the process industries, they will permit customers' technicians to operate the plant themselves and to carry out tests and observations in complete privacy.

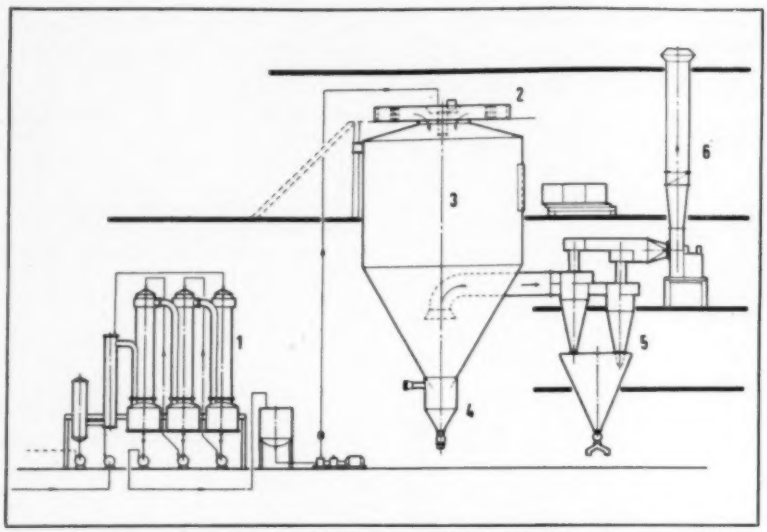
The LUWA spray dryer is designed either for independent co-current or countercurrent air flow operation. No matter what system is adopted, however, all installations comprise the following essential features:

1. Device for the production of a spray and the transfer of the feed liquid.
2. The production of hot air for drying and its transfer to the drying tower.
3. The drying tower itself.
4. Removal of the finished product from the tower; removal of the exhaust drying air; and the recovery of the powder carried away in the air stream.

The Luwa spray drying range utilising the spinning disc method of atomisation starts with a laboratory size unit possessing a capacity of 25 lb./hr. of water evaporation. It has a diameter of approximately 9 ft. and is built complete as a small unit ready for despatch. At the other extreme is a unit with a chamber diameter of approximately 23 ft. and a capacity of 3,000 lb./hr. of water evaporation.

Nozzle type spray dryers usually cater for considerably larger capacities and units of up to 2-4 ton/hr. water evaporation can be produced.

Luwa spray dryers are currently producing foodstuffs, chemicals, pharmaceutical products, soaps and synthetic detergents. Special techniques and plant have been evolved which have resulted in the development of light and heavy duty detergents in hollow bead form.



Layout of Luwa spray dryer plant for free flowing powder. 1. Evaporators. 2. Air inlet and atomising unit. 3. Drying chamber. 4. Powder cooler and main outlet. 5. Cyclone group and powder bunker. 6. Exhaust fan and chimney.

▶LABELLER SEALS FLAT BOXES

The normal method by which a semi-automatic labelling machine applies a label to a container is by pressing the gummed label on to the container from the top or from the sides by one or two press or wiping movements, and in some cases a rubber roller is employed.

Faced with the problem of applying a label, gummed all over, to the top, side and bottom of a flat box, Purdy Machinery Co. Ltd. decided that this could be achieved with a modified version of their semi-automatic *Universal* machine. Modification was made to the feed and wiper mechanism whereby a top and right-angle press for the box together with an under wipe for the underside of the label was carried out simultaneously.

The complete box size range is covered by only one adjustment on the machine.

This can be clearly seen in the illustration and takes the form of an adjustable guide which centralises the labels to the varying box sizes.

▶SILICA ANALYSER

The E.I.L. silica analyser model 58A is claimed to be the first commercially available automatic instrument that continuously analyses the silica content of boiler feed water. The instrument eliminates the tedium and uncertainty of manual determinations and thereby ensures that the boiler feed water is monitored sufficiently frequently and rapidly to enable steps to be made immediately to reduce the silica content. The Silica Analyser is essentially a colorimeter in which the colour of a solution to which reagents have been added is a measure of the concentration of silica in that solution.

▶ECONOMICAL AIR CONDITIONER

The specialised Air Treatment section of AEI-Birlec Ltd. has gained a reputation for the design and installation of plant to meet the most rigorous industrial requirements for humidity and temperature control.

There are, however, cases in which a simpler approach is fully satisfactory and cheaper. To meet these needs the *Frescon* air conditioning unit has been developed and tested by Birlec. It is now available as a compact, self-contained, packaged plant for a wide range of applications, requiring only to be placed in position and connected to electric power and water service.

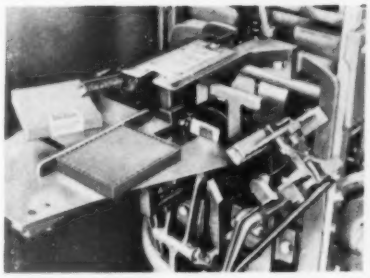
In standard form the *Frescon* is a simple, efficient and highly economical means of limiting relative humidity and temperature. It will maintain room conditions steady for indefinite periods without attention. It is ideally suited for conditioning factory areas, stores, laboratories, instrument rooms, etc.

The unit is contained in a compact sheet steel cabinet divided into lower, middle and upper sections. Air from the room is drawn in through the middle section and passed through a refrigerated element and discharged back to the room through the top section. Excess moisture is condensed as it passes through the refrigerated element and is drained from a drip-tray.

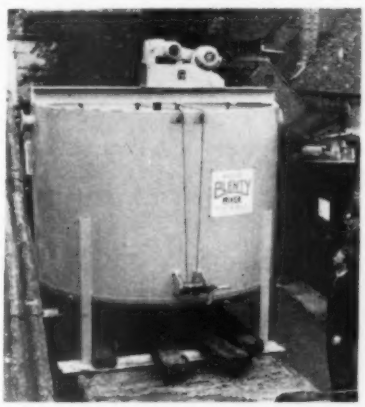
All necessary electrical equipment including a main isolator switch and automatic starters for the compressors and fan motors are built into the cabinet. The compressor is fitted with a safety cut-out to prevent overload. A regulating valve is provided to conserve cooling water supply to the condenser.

▶MIXING UNIT

Plenty and Son Ltd. have operated their plant department for two years, starting in a small way with the supply of tanks, piping, valves, filtering and mixing installations. The range of plant work carried out by this department at Plenty's now includes the design, manufacture and installation of complete plant for storing, metering, mixing and preheating the raw materials for spun resin pipes; plant for pumping, metering and mixing ingredients for animal foods; mixing, heating and homogenising plant for herbicides, bulk fat handling, mixing and storage plant; bitumen emulsion and cutback blenders, and wax polish manufacturing equipment.



Purdy labeller adapted to handle end-seal labels on flat boxes.



One of five Plenty paddle mixers in 2,300-gal. tanks supplied to Gartons of Battersea. The winching gear draws the paddles out of the starch slurry and allows them to mix at correct height irrespective of liquid level.

The Frescon, a new economical air conditioning unit.

The latest addition to their range of equipment is the starch slurry mixing unit. The mild steel Plenty two-blade paddle mixer is driven by a 3 h.p. motor through a worm gearbox mounted above the 2,300 gal. tank. The paddles rotate at 25 r.p.m. to prevent the starch from setting.

The most important feature is the lifting gear, operated by winch on the outside of the tank. This controls the height of the mixing paddles inside the tank, so that however empty or full the tank is the paddles will be at the correct height to keep the slurry on the move. This lifting gear has two other great advantages: when the slurry has been left for a weekend and settled out, the paddles can be lowered gently into the tank to mix all strata gradually. Since the paddles can rise and fall on the mixer shaft rather than the whole shaft rising with the paddles, the five vats can be accommodated inside a building with 10 ft. headroom.

The mixer is designed to deal with 2,300 gal. in 15 min.

▶DUST COLLECTOR

The Sturtevant high efficiency *Cyclone* dust collector is recommended for treating dusts consisting of a large proportion of particles coarser than 15 microns. It is reasonable in installation costs, economical in operation and requires little space.

The principle of centrifugal dust collection has long been popular, but modern procedure enables investigation of every facet of a dust-collecting problem to be made in the laboratory, emulating as closely as possible the actual site conditions and making the necessary adjustments to produce the highest measure of efficiency in dust collection and consumption of power, together with low general maintenance. From the collected data, a suitable cyclone is designed and built.

Sturtevant *Cyclone* dust collectors are used in all types of industry and the company operate their service according to customer requirements by laboratory evaluation of individual dust problems. From client's information, Sturtevant are able to put forward proposals as to the type of dust collector most suitable for the purpose.

American Commentary

NEWS AND VIEWS OF THE U.S. PHARMACEUTICAL INDUSTRY **by Dr. Rudolf Seiden**

Stricter import control on drugs ★ Output and sales of medicinals ★ Antibiotic manufacturers rebut charges

FDA tightens import control

IMPORTS of foods, drugs and cosmetics are now being more thoroughly scrutinised than ever before, reports the Food and Drug Administration. For example, 1,550 shipments to the port of New York over a 3-month period in the summer of 1961 were examined and 283 detained because they did not meet standards set by the Food, Drug and Cosmetic Act.

Intensified inspection by the FDA makes it more important than ever that firms exporting to the U.S. give careful consideration to the FD&C Act and its interpretations (the most recent ones we try to report in this column).

Drug output and sales

U.S. output of medicinals reached 120·1 million lb. in 1960, 12·7% more than in 1959. Greatly increased were streptomycin and penicillin salts, but tetracycline and antibiotic specialties for feeds, food, and crop spraying declined. The total sales of medicinals in 1960 (1959) amounted to 87·9 (87·3) million lb., valued at $557 (582) million.

Antibiotics were the most valuable medicinals produced in 1960. Total output for human and veterinary use was 2·8 (2·3) million lb. Sales were 2·2 million lb., valued at $323·6 million, or 10% larger than in 1959 in quantity, but only 1·79% larger in value. Production of penicillin salts alone amounted to 498 (430) trillion international units and sales were 387 (371) trillion units, valued at $53·4 (57·3) million.

Output of dihydrostreptomycin amounted to only 392,000 (470,000) lb.; sales were 363,000 lb. valued at $8·2 million.

Production of streptomycin increased to 605,000 (from 281,000) lb., while output of tetracycline declined to 287,000 (307,000) lb. Combined output of other medicinal antibiotics, such as chlortetracycline, chloramphenicol, erythromycin and oleandomycin, amounted to 792,000 lb. with sales of 668,000 lb. valued at $175 million.

Production of antibiotics for animal feed supplements, food preservation and crop spraying amounted to 1·2 (1·4) million lb.

The vitamin output in 1960 was the same as in the year before: 11 million lb. Sales of all vitamins totalled 8 million lb. valued at $68·7 million.

The output of sulpha drugs was only 5·1 (5·8) million lb.

Aspirin was again the product manufactured in largest quantity in 1960: 23·6 million lb. Production of barbiturates totalled 852,000 (819,000) lb., and production of all tranquillisers fell to 1·2 (from 1·47) million lb.

Antibiotics anti-trust suit

Pfizer, American Cyanamid and Bristol-Myers are accused by the U.S. government that they conspired to restrain trade, monopolise antibiotic production and sale, and fix prices (see M.C. September, p. 434).

Pfizer have released the following information:

(1) *The Price Fixing Charges*

"The cold, hard logic of the situation is that substantial uniformity of prices among competitors is more likely than not to evolve as a consequence of the working of vigorous competition. A level of prices finds itself as a result of strong competition, and then, through individual commonsense conclusions, tends to be maintained. . . .

"Aureomycin was introduced in 1948 at a price to retailers of $15 for 16 capsules. The following year, just before Parke-Davis introduced Chloromycetin . . . the price was brought down to $10 for 16 capsules. In the following year, prior to the introduction by Pfizer of Terramycin . . . the prices of aureomycin and Chloromycetin were reduced to $8. Terramycin was introduced in March 1950 at $8.40 for 16 capsules. A month later, when Parke Davis reduced its price of Chloromycetin to $6, Pfizer met the price and so did Cyanamid. During the following year Pfizer reduced the price to $5.10, which was matched by Cyanamid and Parke Davis within a few days. After this series of substantial reductions from $15.00 to slightly over $5 published prices of broad spectrum antibiotics tended to level off, but active price competition continues in many ways; for example, through the use of free goods and repeated price cutting on bids to hospitals, government agencies and other institutions."

(2) *Patent and Licensing Charges*

"The anti-trust suit charges that licences between Pfizer and Cyanamid, which were in settlement of an interference proceeding, and the subsequent licensing of Bristol-Myers, Olin Mathieson and Upjohn were such as to constitute violation of the Sherman Act.

"A judgment here must guard against the notion . . . that the very fact that companies settle legal controversies by compromise of conflicting patent claims involves something wrong. . . .

"Pfizer applied for a patent on Tetracycline in October 1952. In March 1953 Cyanamid applied for a patent on the same drug. A question arose as to who had come up with the discovery of the new drug. As is customary in such a situation, the Patent Office, after a preliminary determination that tetracycline was patentable, declared an 'interference.' . . . The companies decided that, rather than go through a long, costly, and cumbersome interference proceeding, they would . . . try to determine who had prior right to the patent, and that the company with prior right would license the other to make and sell the drug. Pfizer was found to have the prior right, and under the agreement licensed Cyanamid to manufacture and sell the drug. . . . The Department of Justice . . . reviewed . . . these licence agreements in the spring of 1955 and did not challenge them in any way."

Heavy advertising keeps detergent prices low, say Hedleys

A powerful defence of their heavy advertising expenditure is made by Thomas Hedley and Co. in their financial statement for the year to June 30. The essence of their argument is that it is an instrument of competition. "If one believes in competition, it is quite illogical not to believe in advertising."

Hedleys admit that advertising enters into the cost of a product, but reaffirm from experience the classic argument that because advertising creates a mass demand it makes possible mass production and a consequent lowering of costs and prices. If the prices of their washing powders had risen in line with general price increases since 1950, the housewife would now pay 2s. 3d. a packet instead of 1s. 10d. That was one result of advertising. Another was exports. Hedleys' exports now stand at £3 million a year, ten times the figure in 1951. Strong exports depended on a strong home market, which again depended on effective advertising. Hedleys also attribute the general rise in standards of cleanliness to extensive advertising of washing products, and point out that the *per capita* usage in Britain increased by 26% from 1951-60, the period following the ending of soap rationing and the consequent increase in advertising and competition.

No tax. In conclusion Hedleys attack proposals that advertising should be taxed. "If the cost of advertising should be increased disproportionately by taxation some other basically less efficient and currently more costly method of selling the consumer would have to take its place."

Profits doubled. Since 1954 Hedleys profits have more than doubled, from £1,151,000 (after tax) to £2,708,000. In ten years wages of their workers have almost exactly doubled.

The company spent over £1 million on research in 1960-61. Current assets are £14·9 million (£12·2m).

Hedleys are the British subsidiary of Procter and Gamble, whose profits to June 30 increased from £35 million to £38 million, after tax.

M. o. H. may be challenged in court

The Association of British Pharmaceutical Industry has taken counsel's opinion on the legality of the action of the Minister of Health in buying patented drugs from unlicensed makers. He is doing this by invoking section 46 of the Patents Act, which allows the Government to use patented goods for "the services of the Crown." The question is: is the purchase of drugs for hospital patients a "service of the Crown?" Legal opinion seems divided.

It is likely that the four firms whose drugs are involved—Parke Davis, Pfizer, Merck and Lederle Laboratories—have also taken counsel's opinion. According to the *Daily Telegraph* the Minister's action may soon be challenged in the courts. If this is done it will be by one or more of the aggrieved firms, not by the A.B.P.I., which could not, of course, bring such an action.

By buying tetracyclines, chloramphenicol and chlorothiazides from "pirates" abroad the Minister hopes to save £350,000 a year, less royalties he will pay to the patent holders. The extent of the saving is uncertain, therefore.

Chemical plant expansion

Construction of a maintenance engineering and welfare block for Whiffen and Sons Ltd. at Loughborough is nearing completion. The building provides accommodation for engineering staff, and drawing offices, workshops for joiners, electricians and other technicians, and a welfare section. The two-storey building, costing £48,000, has 9,000 sq. ft. of floor area.

It is part of a £300,000 development scheme. Work is in progress on reconstruction of general plant and on buildings for the manufacture of a wider range of dye-line chemicals. Work is expected to commence shortly on plants for the manufacture of cyanuric acid and trichlorisocyanuric acid.

Drug company moves

Baxter Laboratories Ltd. have moved their Wallerstein Division and Wheeler and Huisking Division to their new factory and offices at London Road Trading Estate, High Wycombe, Bucks. The manufacture and distribution of industrial and pharmaceutical enzymes will be carried out from High Wycombe.

A. T. Wheeler and J. F. Potton remain on the board of the company but will be taking a less active part in day-to-day activities. As a result of their reduced activity it has been decided to discontinue trading in crude botanical drugs.

A. M. Hamilton, B.SC., F.P.S., as director and general manager, will be responsible for the pharmaceutical and chemical divisions of Baxter Laboratories Ltd.

B.D.H.'s partner earns more

Mead Johnson, the American pharmaceutical company which recently acquired a 35% interest in British Drug Houses and markets the slimming preparation *Metercal* in the U.K. have announced higher earnings for the first half of 1961. Earnings a share were $2.98 against $2.78 in the same period of 1960.

More petrochemicals

In the first six months of this year the oil industry supplied 795,227 tons of chemical feedstock, 4% more than in the preceding six months. 99,302 tons of propane and butane were supplied, 37% more than in the foregoing six months. Total consumption of oil products in the U.K. reached 23,171,887 tons, 9·2% more than in the comparable period in 1960. These figures were published by the Petroleum Information Bureau.

CHANNEL SWIM

A complete food powder developed by Glaxo Laboratories as an easily-prepared, nourishing tube feed for hospital patients unable to eat normally helped sustain 17-year-old Margaret White, of Leigh-on-Sea, Essex, when she swam the Channel recently—the youngest to complete the crossing. During the 21-mile swim in thick fog and icy water, completed in 15 hr. 8 min., she took the food, Complan, mixed as a drink with hot milk.

Thomas Kerfoot and Co. Ltd. announce that **Leigh H. Kerfoot** has been appointed a director. He is the great-grandson of Thomas Kerfoot, and the only son of Dr. T. H. M. Kerfoot, joint managing director of the company. He has spent two and a half years in the U.S., where he worked with Eli Lilly and Co., Wyeth International Ltd. and the S. J. Stokes Corporation.

Dr. D. H. Sharp has been appointed Director (Technical) of the F.B.I. as from November 1. He will take up the appointment on the retirement of the present technical director, **Major-Gen. Dove**. At present Dr. Sharp is assistant to one of the managing directors of Fisons Ltd. When Pest Control Ltd. was acquired by Fisons Ltd. in 1954 he was works manager at Harston. Dr. Sharp, who is 44, is an honours chemistry graduate of London University.

Prof. E. R. H. Jones, F.R.S., of Oxford, has been chosen by the American Chemical Society to receive the 1962 Fritzsche Award. Prof. Jones, who has held the chemistry chair at Oxford since 1955, is referred to as one of the world's foremost organic chemists. The Fritzsche Award was granted to Prof. Jones for his outstanding contributions to terpenoid chemistry—notably the chemistry of the higher terpenes and the synthesis of terpenoids related to vitamin A. His work has been authoritatively termed a classical break-through in terpene chemistry, which has proved to be of enormous structural as well as biogenetic significance. The presentation to Prof. Jones of the Award's gold medal and cash prize by a representative of Fritzsche Brothers Inc. will take place at the spring meeting of the American Chemical Society to be held in Washington May 20-29, 1962.

S. C. Johnson and Son Ltd., wax polish manufacturers, have appointed **Dr. Keith Sellars** as director of research and development.

Fisons Ltd. have announced the following appointments to the boards of subsidiary companies:

G. V. K. Burton, chairman of Fisons Overseas Ltd.;

A. Gillies, managing director of Fisons Fertilizers Ltd., also acting chairman;

H. G. Rope, vice-chairman of Fisons Fertilizers Ltd.;

Dr. E. Parry-Jones, chairman of Fisons Pest Control Ltd.; and

A. Robinson, deputy chairman of that company.

W. C. d'Leny.

W. C. d'Leny has been appointed chairman of Billingham Division, I.C.I., following the death of **W. J. Ward.**

Mr. d'Leny joined Billingham in June 1926. He became the Billingham Division research director in November 1951, and in January 1958, following the reorganisation which resulted in the formation of the new Heavy Organic Chemicals Division, he was appointed Billingham Division joint managing director (technical).

He was educated at Alleyns School, Dulwich, and St. John's College, Oxford, and lives at Greatham, near West Hartlepool in County Durham. He and his wife enjoy winter sports holidays and his other interests include farming and the theatre.

Glovers (Chemicals) Ltd. announce that **V. C. H. Brockwell,** who was formerly southern technical sales manager, has been appointed general sales manager, and that **M. Bell** has been appointed technical service manager.

Bayer's chairman dies

Dr. Ulrich Haberland, chairman of Farbenfabriken Bayer A.G. of Leverkusen, died suddenly from heart attack on September 10. He was 60.

Haberland was a chemist and he joined I.G. Farbenindustrie in 1928. Nine years afterwards he became manager of the Uerdingen works and in 1945 he became a director of I.G. Farbenindustrie.

Haberland was faced with his greatest crisis in 1945 when Germany capitulated and I.G. Farbenindustrie was broken up. For six years he strove to combine four former I.G. Farben works on the lower Rhine, and in 1951 it was possible to re-establish Farbenfabriken Bayer. Today the company employs 60,000 people and produces annually 13,000 different products, valued at about £275 million.

Haberland worked hard for the welfare of his employees and built more than 17,000 homes for them, besides initiating a share-buying scheme under which today more than 20,000 employees hold shares in their own company.

Dr. Harold H. Zeiss, formerly of Monsanto Chemical Co.'s research and engineering division, has been elected president and director of Monsanto Research S.A., Zurich, Switzerland. He was formerly an assistant professor at Yale University and has established a national reputation in organometallic chemistry. He has been granted 12 patents and has 10 additional patents on application. His "Organometallic Compounds," an American Chemical Society monograph, was published in 1960.

The Committee of Privy Council for Medical Research have appointed **Prof. M. L. Rosenheim** (Professor of Medicine in the University of London at University College Hospital Medical School) and **Prof. Wilson Smith** (lately Professor of Bacteriology in the University of London at University College Hospital Medical School) to be members of the Medical Research Council.

Following a recent illness, **D. R. Mackie,** at his own request, has resigned from his position as managing director of Monsanto Chemicals Ltd. He continues as a member of the board. Mr. Mackie will be succeeded as managing director by **John C. Garrels,** Jnr., deputy managing director, who has been carrying out the duties of the office since Mr. Mackie's illness in March. Mr. Garrels joined Monsanto Chemicals Ltd. from the Plastics Division of its American parent company at the beginning of 1961.

Dr. David Train has resigned his Readership in Pharmacy in the University of London and is joining Cremer and Warner, consulting chemical engineers, as a partner.

British Petroleum's new chemical laboratories

The first two laboratory buildings specially constructed for the chemicals division at the BP Research Centre, Sunbury, are now complete.

The new laboratories with their equipment cost about £500,000.

The No. 1 chemicals division laboratory building has four storeys and a floor area of about 38,000 sq. ft. In it are 24 individual laboratories, including three in which constant temperature can be maintained. An annexe to this building houses the high-pressure laboratory which is a self-contained unit with three control rooms, six small laboratories and a workshop.

The No. 2 chemicals division laboratory building is specially designed for work on pilot plants and has been built to allow for future extensions.

Vials and closures for antibiotics

New vials, closures and labels for their injectable antibiotic products have been introduced by The Distillers Co. (Biochemicals) Ltd. Two new vials of improved design form the basis of the project. One is a general purpose injection-type container for the lower strengths and the other a new type of multi-dose container. The adoption of these vials has enabled better closures to be developed. These consist of one size of aluminium seal and one size of rubber disc.

Advantages of the rubber discs, which are of a unique plano-convex shape, include resistance to moisture, much easier needle penetration and excellent re-sealing characteristics, thus providing protection for the products even in tropical conditions. Unlike ordinary rubber stoppers there are no thick shoulders to the discs so that if a needle is inserted at an angle, problems of blocking and difficult penetration do not occur. The rubber composition of the discs has been formulated to give maximum compatibility with the individual products.

The aluminium seals have been designed with larger apertures which cater for the insertion of two needles simultaneously through the rubber discs. With the rubber discs the aluminium seals constitute very effective vial closures. Tests have demonstrated that vials bearing the closure and filled with air under a pressure of 60 lb. have not lost any entrapped air after storage.

The new packaging has become available with the introduction of *Soluvone*, an injection containing crystalline sodium penicillin G and streptomycin sulphate.

Laminating machine

Gordon and Gotch Ltd. has acquired the world distribution rights of the *Alpine* laminating machine.

The machine, which is manufactured in four widths, 18 in., 24 in., 40 in. and 50 in., can laminate sheets of any size up to the width of the machine and any length in a continuous action. It can be used for applying cellulose film to either cellulose film, pliofilm or polyethylene; polyethylene to foil or paper; paper to foil. Glue is automatically-fed for double laminating action.

Polythene nozzle tubes

Flexile Metal Co. have developed an entirely new tube for eye ointments and intramammary creams. It is essentially a *simple* extrusion. The extrusion is as for a standard No. 80 short screwed nozzle tube, but instead of a threaded nozzle a groove is introduced into the boss at the base of the nozzle to take a snap-on polythene nozzle. The polythene nozzle has an elongated 16 mm. parallel sided canula which is sealed by a 16 mm. push-on cap.

Group of Venesta extruded aluminium containers for the packaging of Ciba products. All the containers are lacquered internally, the rigid cans have aluminium caps embossed "CIBA." A variety of colour schemes help chemists identify products at a glance.

The soft polythene tip of the canula nozzle is particularly suitable as an applicator to infected areas where a delicate application is called for and where a metal nozzle might have a tendency to scratch. This new style eye ointment and intramammary cream tube has the great advantage that it can be produced in tin, tin-coated lead, aluminium or as an aluminium tube *internally lacquered*. This versatility is particularly important because with many of the new antibiotic preparations, tin tubes with their minute traces of copper have not proved to be entirely satisfactory and, therefore, aluminium tubes have been requested. If aluminium tubes without internal lacquer are used corrosion might occur. The new tube should enable a wider range of products to be developed for intramammary and eye ointment uses. Flexile state that considerable savings can be achieved with the new tube in aluminium compared with an elongated nozzle aluminium tube. In pure tin the prices of the new tubes are comparable to pure tin elongated nozzle tubes.

New style polythene nozzle tubes by Flexile Metal are used for eye ointments and intramammary creams.

Parke Davis are using the new tube for *Mascetin* ointment.

Multiwall sacks

A booklet giving advice on the choice of multiwall paper sacks has been published by the Association of British Chemical Manufacturers. Attention is drawn to the variable components which go towards the make-up of these sacks. By selecting the correct components it is often possible to make economies and improve performance. The booklet costs 21s. post free, cash with order, which must go to A.B.C.M., 86 Strand, London, W.C.2.

Napkin washing aid

Free sample sachets of *Napisan*, a new product of Gascoigne-Crowther Ltd., are being made from cellulose film coated with polythene.

The product is designed to obviate the need for boiling babies' napkins, and it is claimed that soaking in a solution of Napisan and lukewarm water kills germs, destroys odours and removes stains. A 2s. 6d. packet should last 3 weeks.

The sachets, measuring 4 in. × 3¼ in., contain enough for two average washes. They are filled and heat sealed from the reel. Printed lettering in a double frame is flexographic in light blue, thrown into contrast by the background of white powder showing through clear film.

News from Abroad

SOUTH AFRICA

Vaccine laboratory

Work has begun on a new £67,500 Government Vaccine Institute at Pinelands, near Cape Town. The building will be bigger than the present institute at Rosebank, Cape Town. The Institute, the only one of its kind in Southern Africa, produces smallpox vaccine for use in South Africa, the Protectorates, the Federation and in Portuguese East Africa. The new building will house sheep and laboratory animals needed for producing the vaccines. It is expected to be ready about the middle of 1962.

Wholesalers v. manufacturers

A wholesale chemical firm decided at a meeting in Johannesburg that none of the retail chemists tied to it by agreements would, in future, stock the products of an American firm of manufacturing druggists which decided on July 1 to supply direct to retailers. This is the second important drug manufacturer to cut out the middleman. Since nearly half the wholesalers' profits come from the 15% commission they get from the manufacturers, their profits are being seriously reduced. This resolution was described as a boycott by drug manufacturers and other retail chemists. They said it was unethical.

The wholesalers, they said, were able to bring pressure to bear on the retailers because of tie-up agreements. The tie-up works as follows: A qualified pharmacist is given shop fittings and allowed extended credit and loaned comparatively large sums of money to tide him over, provided he undertakes to buy two-thirds of all his requirements from the wholesaler. When a drug supplied by a "non-co-operative" manufacturer is prescribed, the patient is asked to call back later. The pharmacist then telephones the doctor and tells him that the drug is not in stock and asks permission to substitute one supplied by the wholesaler to whom he is tied. The doctor often agrees. Competition between wholesalers has become so keen that some independent retailers are using them as warehouses and carry only meagre supplies. When a drug is prescribed they telephone a wholesaler and demand immediate supply.

CANADA

Potash project

Borax (Holdings) Ltd. announce that its American operating company, United States Borax and Chemical Corporation, has entered into a joint venture with Homestake Mining Co., of San Francisco, California, to complete studies relating to possible potash production in Saskatchewan, Canada, where U.S. Borax has been investigating permits held since 1957.

U.S. Borax, with mines at Carlsbad, New Mexico, is today the second largest producer of potash in the U.S.A. Homestake Mining has had extensive experience in gold and uranium mining.

HONG KONG

Cyanamid patent infringement

A pharmaceutical firm in Hong Kong has been permanently restrained from selling the drug sulphamethoxypyridazine. The drug was developed by Cyanamid's Lederle Laboratories and is sold under the trade name of *Lederkyn*.

A consent decree, arising out of a complaint filed by American Cyanamid Co., enjoined T. W. Wu and Co. from selling the drug in violation of Cyanamid Hong Kong patent No. 11 of 1958.

GHANA

Hungary sponsors pharmaceuticals

The Complex Hungarian Trading Co. is reported from Accra by Barclays Bank D.C.O. to be establishing pharmaceutical and cable plants in Ghana. The pharmaceutical plant will have an annual capacity of 1 million ampoules and 1,000 million tablets and the cable plant an annual capacity of about 3,600 tons. Under an agreement signed between the Government and the company, Ghanaians are to be trained in the installation and operation of the plants.

ISRAEL

World's largest bromine plant

The bromine factory at Sdom, which is reported from Israel by Barclays Bank D.C.O. to be due to come into full production this autumn with an anticipated annual output of 10,000 tons, will be the biggest of its type in the world. Its entire production of bromine and bromine products until the end of 1962 has been sold in advance.

HUNGARY

"Mud and herbs" cosmetics

Inspired by a report of a British cosmetician on the treatment of injuries with herbal compresses, two Hungarian beauty specialists have produced several new cosmetics combining the benefits of herbs and radio-active and other medicinal spa waters.

Separate packs and creams have been prepared for dry and greasy skins. These make use of refined spa mud as well as spa waters mixed with vitamin-rich herbal creams. One cream includes camomile, lavender, lime blossom, peppermint and juniper.

AUSTRALIA

Cyanamid's new factory

The Australian subsidiary of the U.S. firm of Cyanamid has taken an option on 105 acres for a new factory at Laverton, on the southwestern outskirts of Melbourne.

The subsidiary will spend several million pounds on the plant, the first section of which will be manufacturing pharmaceuticals, before the end of this year. Further activities will be undertaken when the market has been surveyed.

Cyanamid-Australia also has a plant in Sydney, which supplies the Australian and world markets with medical products.

Increased tariffs

Increased tariffs now apply to imports of tetrasodium pyrophosphate and sodium tripolyphosphate. Manufacture of these products is relatively new in Australia and past tariffs have been non-protective.

New C.S.L. director

The production manager of the Commonwealth Serum Laboratories, Mr. J. C. McAllester, has been appointed acting director, replacing Dr. C. E. Cook who was appointed when the director, Dr. P. L. Bazeley, was suspended in May, on charges of improper conduct as a public servant.

Expansion plans

The expansion programme of Potter and Moore, Australia, is to be accelerated, as are plans for the associated company, W. J. Bush and Co. (Australia) Pty. Ltd. To this end Mr. A. J. McIntyre, a director of Potter and Moore Ltd., London, has been visiting Australia.

New chemical plant

A plant to produce about £150,000 worth of caustic soda and chlorine a year is to be erected near Fremantle by Chemical Industries (Kwinana) Ltd. At present Western Australia imports all its caustic soda and chlorine from the Eastern States.

HONDURAS

Detergent and chemical plant

The Inter-American Development Bank has approved a U.S. $360,000 loan to Quimicas Dinant de Centroamerica of Tegucigalpa, Republic of Honduras, to help finance the installation over five years of a plant for the manufacture of detergents, soap powders, disinfectants, industrial chemicals and other products.

Announcing

Type E.101

the most advanced deioniser in the world . . .

P6916

the most significant advance since **ELGA** intro

IF YOU USE WATER . . .

the new ***Elgastat*** type ***E.101*** will provide ultra-pure water when and where required

INSTANTLY | 50 gallons per hour—at the turn of a tap.

SIMPLY | by connecting the Elgastat to the nearest tap.

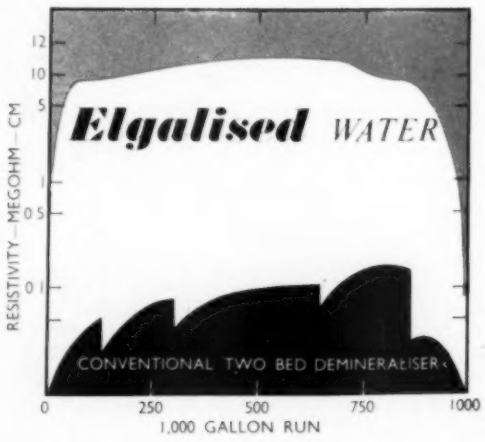
CHEAPLY | at about 1d. per gallon even in the hardest area.

CONSISTENTLY | 1,000 gallons (4,500 litres) between cartridges exchanges.

WITH QUALITY | that never varies.

WITH PURITY | that is not less than 5 megohm-cm.

Contrast Elgastat E.101 with conventional deioniser. Resistivity of elgalised water never varies.



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as compact as a small filing cabinet
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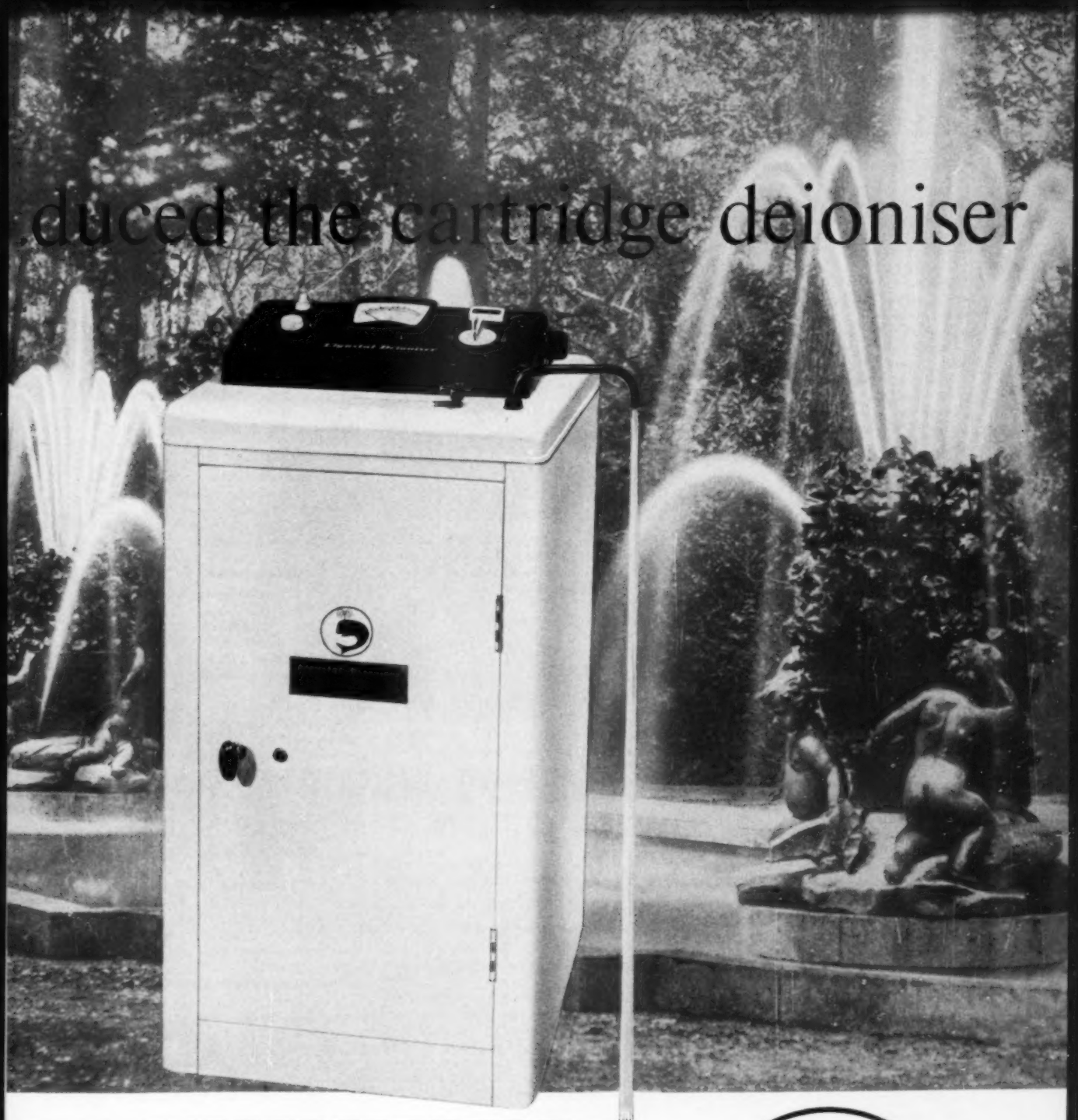

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Name .....

Company .....

Address .....

☐ *Tick here if you would like a demonstration.* M.C.1

TELEPHONE: LANE END 396

"Broad Spectrum" worming drug

Mintic, a drug which enables farmers themselves to treat their cattle and sheep with an oral drench against the whole range of intestinal roundworms causing parasitic gastro-enteritis, has been developed by I.C.I.'s Pharmaceuticals Division as a result of their successful introduction in February of *Promintic*, a new worming drug for administration as an injection by the veterinary profession.

Methyridine, the basic chemical in both products, represents a marked advance on other treatments, including phenothiazine. Its most important feature is that it attacks stomach and intestinal worms at all stages in the life cycle, it is claimed. Other current treatments have little or no effect against immature forms and a treatment which will remove them represents a significant advance.

Unlike phenothiazine, which is a valuable drug in the treatment of certain stages of worms, *Mintic* has a wide range of activity and will thus make up for some of the deficiencies of phenothiazine. *Mintic* is not, however, active against tape worms or liver fluke.

The cost to the British farmer will depend on the age and weight of the animal to be treated. For example, the cost of dosing a full-grown ewe of the heavier breeds will be 2s., and for the smallest lamb 4d. For a yearling calf weighing about 3 cwt. the cost would be 6s.

These costs, when related to the market value *at the time of dosing*, amount to something less than 1%, and, of course, very much less as a proportion of value of the animal in prime marketable condition.

Volumetric concentrates of lab. chemicals

May and Baker Ltd. have introduced a range of standard volumetric concentrates packed in plastic ampoules which are both labour-saving and easy to handle. Each ampoule contains concentrate sufficient to make 1 litre of standard solution to the specification described. In use, the *Volucon* ampoule is placed in the neck of the volumetric flask and the funnel provided is fitted over the upper stem of the ampoule.

The upper and lower diaphragms of the ampoule are broken in one movement with the plastic piercing rod. The tapered portion of the rod, together with the seating of the lower stem of the ampoule, forms a valve so that the ampoule can be completely filled with distilled water for rinsing. A second wash removes all remaining traces of the concentrate and the solution in the volumetric flask can then be made up to the graduated mark. The ampoule remains in the same position throughout,

Making up a standard solution of a laboratory chemical with the new volumetric concentrate packed in a plastic ampoule.

and there is no risk of losing any material by handling.

Concentrates packed in this way at present include N/10, and in some cases N/1, solutions of 15 commonly used laboratory chemicals, including hydrochloric and sulphuric acids, sodium and potassium hydroxide, sodium carbonate, oxalic acid, sodium thiosulphate and potassium bromide.

Although the ampoules are designed to make up 1 litre of stock solution, the normality can be altered simply by changing the size of the volumetric flask.

Each *Volucon* pack contains six ampoules, one plastic funnel, one piercing rod and six labels.

Antibacterial skin powder

The Distillers Co. (Biochemicals) Ltd. have introduced *Zynotracin* powder for topical application in common bacterial skin infections. Each gram contains 4·5 mg. xanthocillin and 500 i.u. zinc bacitracin. The product is issued in plastic puffer packs of 5 g. and may be supplied upon prescription only. Trade price for pack of 5 g., 3s. 8d., ex P.T.

Oxidase inhibitor

Drazine (phenoxypropazine hydrogen maleate), a new monoamine oxidase inhibitor of entirely British origin, is being introduced to hospitals only by the manufacturers, Smith and Nephew Ltd. The compound is available in 5 mg. white tablets embossed with the letters SNP for ready identification. *Drazine* is presented in bottles of 100 and 500 tablets at a basic N.H.S. price of 15s., and 58s. respectively, subject to P.T.

Synthetic organic acids

A new group of synthetic organic acids developed after extensive research by the Shell laboratories in Amsterdam is now available under the trade name *Versatic*, from a pilot plant, and will be produced on a commercial scale from January next.

Although similar in some respects to other organic acids already on the market, Shell say that the new acids possess unique properties which will find applications in the surface coatings, plastics, rubber, metallurgical and other industries. They are produced from olefines, carbon monoxide and water by a process developed by Shell from the original work of Dr. H. Koch, of the Max Planck Institut fuer Kohlenforschung, at Muelheim, Ruhr, Germany.

A £2 million plant to handle the acids when they go into commercial production is now under construction at Shell's large oil and chemical refinery complex at Pernis near Rotterdam.

Timber preservative

Successful wood preservation depends on getting an adequate amount of preservative deep into the wood. A technique of achieving this without pressure impregnation, dipping or spraying has been developed. It relies on the use of a new type of preservative formulation called *Woodtreat*. It consists of pentachlorophenol incorporated in a mayonnaise type emulsion. This thick emulsion is applied to the surface of timber as an overall coating or as spaced bands or ribbons, and provides a reservoir from which the preservative is gradually released and absorbed by the timber. It can be considered, therefore, as a method of soaking timber without the use of soaking tanks. A ¼ in. layer of *Woodtreat* is claimed to be better than the application of 20 brush coats of organic solvent type preservatives. The makers of the new product are Preservation Developments Ltd.

Anti-emetic suppositories

Burroughs Wellcome and Co. have added suppositories and paediatric suppositories to their *Valoid* range of anti-emetic products.

They are recommended for the prophylaxis and treatment of all forms of nausea and vomiting whenever the oral and parenteral routes are precluded. Each suppository contains 100 mg. cyclizine hydrochloride in 1·8 gm. hydrogenated fat base. Each paediatric suppository contains 50 mg. cyclizine hydrochloride in 1 gm. hydrogenated fat base.

Both products are issued in packs of 10 suppositories in individual plastic cones, at a price of 15s. for 10 (plus P.T.) and, for the paediatric suppositories, 12s. for 10 (plus P.T.).

MEETINGS

Pharmaceutical Society

October 12. "Biological and Non-Biological Models of Drug Receptors," by A. H. Beckett. 7.30 p.m. 17 Bloomsbury Square, London, W.C.1.

November 23. "Pharmaceutical aspects of a journey through Australasia and the United States," by Dr. W. Mitchell. Evening. 17 Bloomsbury Square, W.C.1.

Institution of Chemical Engineers

October 19 and 20. The 1961 symposium of the Graduates and Students Section. "Scale-Up and Pilot Plants." 9.15 a.m. Royal Overseas League, St. James's, London, S.W.1.

Society of Chemical Industry

November 3. Fine Chemicals Group. "The Wittig Reaction and its Application in Organic Synthesis," by Prof. B. Lythgoe. 6.30 p.m. 14 Belgrave Square, London, S.W.1.

Society of Instrument Technology

October 19. "The Inspiration of Science," by Sir George Thomson. 6.30 p.m. 26 Portland Place, London, W.C.1.

November 15. "Instrumentation at Low Temperatures," by Dr. R. Chambers. 7.30 p.m. Department of Physics, University of Bristol, The Royal Fort, Bristol 8.

Society for Applied Bacteriology

October 24. Presidential Address: "The Philosophy of Disinfectant and Antiseptic Evaluation," by G. Sykes. 4 p.m. Queen Elizabeth College, Campden Hill Road, Kensington, W.8.

The following demonstrations will be shown from 5.30-7.30 p.m. in the Sir John Atkins Laboratories, Queen Elizabeth College:

DISINFECTION AND STERILISATION

1. The testing of surfaces for bactericidal action, by D. Kingston and W. C. Noble.

2. A comparison of two methods of evaluating sanitisers with special reference to a source of variation from neutralisation, by A. H. Walters and T. G. Mitchell.

3. Assessment of the effect of disinfectants and cleaning agents on bacteria deposited on surfaces, by A. Hurst.

4. A quantitative method for estimating the activity of germicides on skin, by R. C. S. Woodroffe.

5. A method for testing the efficiency of formaldehyde as a sterilising agent for staphylococci, by R. M. Fry.

6. The quantitative assessment of antibacterials and enzymes by the diffusion plate-assay technique, by D. V. Carter.

7. The Berry method for determining mean single survivor time of *Escherichia coli* in a disinfectant, by A. M. Cook.

DISTILLERS' C.D. EXERCISE

A "casualty" being rescued by industrial civil defence volunteers at a recent demonstration given by C.D. units of the Distillers Co. Ltd. at Epsom, Surrey. The demonstration was attended by the Minister of State, Home Office, at the invitation of D.C.L. chairman, Sir Graham Hayman. The company has 900 trained industrial civil defence people in its service.

8. From laboratory to field—a study in correlation, by A. F. Hams.

9. Ionising radiation used for the elimination of salmonellæ in foods, by B. M. Freeman.

GENERAL

10. Sectioning bacteria for electron microscopy, by A. M. Glauert.

11. Rotating soil percolator, by W. K. Smith.

12. Automated microbiological analysis, by J. F. Marten.

13. An improved selective and diagnostic medium for isolating coagulase positive staphylococci, by A. C. Baird-Parker.

14. Luminous bacteria, by R. Spencer.

New drugs under old names

The Advertising Association has considered whether it is legitimate to retain the original brand name of a medicinal product which has been entirely reformulated and offered to the public for a different purpose.

The new advertising could be misleading because people accustomed to taking the product in its original form may go on buying it without knowing that the formula has been changed. It could also be dangerous because doctors may not be aware of the new formula, and if they are, they may not know which version the patient has been self-prescribing and taking.

For these reasons the Advertising Association says that when both the formula and purpose of a medicinal product are changed, the brand name should also be changed. Member companies of the Advertising Association have been notified accordingly.

Government helps new industries in Eire

The Eire government is intensifying its campaign to attract industries to the country. The Irish Industrial Development Authority's chairman, Dr. J. P. Beddy, told a conference in London that incentives to industrialists include non-repayable grants of up to the full cost of the site and the buildings plus half the cost of plant and machinery plus the cost of training workers. Tax concessions are also given.

From 1952-60 grants amounting to £4·1 million were given for 92 projects. From March 1960 to March 1961 grants were given for 37 projects to a value of £3·2 million.

Among the new industries established in recent years are four pharmaceutical enterprises, namely Hedley Laboratories (British), Leo (Ireland) Ltd., (Danish), Warner-Lambert (American), and Loftus-Bryan (German).

New HQ for D.S.I.R.

The D.S.I.R. has moved to State House, High Holborn, London, W.C.1, Telephone Chancery 1262.

Advice for prescribers

The third issue of the *Prescribers' Journal*, published by the Ministry of Health, contains articles on sulphonamides and nitrofurans, on anticoagulants, and on new treatments to dissolve intravascular thrombi.

Antibiotic inventor's claim fails

A quarrel about the discovery and development of cephalospirin N, a new antibiotic, has been settled by the Assistant Comptroller of the Patent Office. Dr. H. Burton claimed a half share in the benefits arising from patent 745208. Sir Howard Florey, president of the Royal Society, and five other scientists were co-inventors and they asked the Comptroller to direct Dr. Burton to join them in assigning the patent to the National Research Development Corporation. This has now been done.

The Assistant Comptroller said Dr. Burton's contribution did not justify the half share he claimed. He added that he found it difficult to extract a coherent story from Dr. Burton's evidence, much of which was given over to unnecessary and irrelevant abuse of his fellow scientists. The fact that one member of a team was fortunate to have allotted to him a line of enquiry which led to an important discovery did not entitle him to a bigger share than the rest of the team.

. . . a sales representative in the Mineral Products Department, to be exact. I'm very happy to be here, too. And people have been feeling like that ever since the business started more than ninety years ago. I suppose it's because everybody feels that important things are always happening, every day. Take my department. We provide clays, bonding agents and sand additives for the foundry industry; filter aids for beer, sugar and pharmaceuticals—and processed earths for a whole variety of carrier and filler applications. It's my department, too, that sells many specialized products for the paint industry. In short, we're interested in everything from paper, plastics and printing inks to filtration and foundry work—and a lot more! Yes, in my department, there's always something new going on. At Berk, we feel, we're helping to push progress just a little faster all the time.

If you need information or advice on any chemical problem, ask Berk about it. Somewhere in the wide range of Berk literature, the answer may already exist; and if it does not, Berk experts will gladly set to work to find it. Write or telephone:

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The Chemical Market

LONDON.—Further reductions in the price of **glycerine** by £20 per ton were notified. This is the second reduction within a few months, making a drop of £38 10s. per ton. Metals and salts were in little demand which was reflected in slightly lower prices. The price of **zinc oxide** B.P. came down by £2 10s. per ton, but **sulphate of copper** advanced by £1 to £79 per ton. Crude drugs and essential oils were mainly quiet with slight increases of 6d. per lb. on **menthol** and 3d. per lb. on peppermint oil from Brazil.

FINE CHEMICALS

Acetanilide 2s. 10d. lb. (cwts.)
Adrenaline B.P. £43 15s. kg.
Aluminium hydroxide B.P. 7s. lb. (cwt.)
Aluminium lithium hydride 120s. (100 g.)
Arsenic trioxide £37 ton
Ascorbic acid 51s. kg.
Aspirin 4s. 8d. lb.
Atropine sulphate £59 1s. kg.
Barbituric acid 44s. kg.
Benzoic acid B.P. 2s. 9½d. lb. (cwt.)
Benzyl benzoate 5s. lb. ,,
Bismuth salts
Carbonate 20s. lb.
Subnitrate 18s. ,,
Borax B.P. £60 ton
Boric acid B.P. Gran. £90 10s. ,,
Bromine B.P.C. 6s. lb.
Caffeine 32s. kg.
Calciferol 3s. 9d. g.
Calcium gluconate 3s. 7d. lb.
Calcium glycerophosphate 12s. ,,
Calcium lactate B.P. 2s. 4d. ,,
Chloral hydrate 9s. 4d. kg.
Chloramine T 4s. 2d. lb.
Citric acid B.P. 179s. cwt.
Codeine £138 10s. kg.
D.D.T. Tech. 3s. lb.
2 : 4 Dichlorophenoxyacetic acid £310 ton
Ephedrine hydrochloride 3s. 3d. oz.
Ecualyptol 11s. lb.
Eugenol 21s. 6d. ,,
Ferri ammon. citrate B.P. 4s. 5½d. ,,
Gallic acid B.P.C. 12s. 3d. ,,
Geranyl acetate 17s. 6d. ,,
Gluconic acid 22s. 6d. ,,
Glycerophosphoric acid 4s. 7d. ,,
Glycine 8s. 3d. ,,
Hexamine B.P. 1s. 11½d. ,,
Hexyl Resorcinol 150s. ,,
Hydroquinone 8s. 6d. ,,
Iodine, crude 17s. 4d. kg.
Iodoform 24s. 1d. lb.
Lactose 132s. 6d. cwt.
Lithium carbonate 4s. 10d. lb.
Lysine hydrochloride 23s. (100 g.)
Magnesium carbonate B.P. Heavy 185s. cwt.
Magnesium trisilicate 3s. 1d. lb.
Manganese hypophosphite B.P.C. 12s. 11d. lb.
Mercurous chloride 53s. 6d. kg.
Methyl salicylate 3s. 3d. lb.
Morphine
Nicotinamide 50s. 6d. kg.
Nicotinic acid 32s. 9d. ,,
***o*-Nitro aniline** 18s. (250 g.)
***m*-Nitro aniline** 18s. 2d. ,,
***p*-Nitro aniline** 25s. ,,
Nitrobenzene 1s. 9d. lb.
Paraformaldehyde 1s. 3½d. ,,
Pentachlorphenol 2s. 4d. lb.
Peracetic acid 2s. 8d. ,,
Phenol Ice Crystal 1s. 4d. ,,
Phenolphthalein 9s. ,,
Phosphoric acid B.P. 1s. 4d. ,,
Potassium permanganate B.P. 2s. 0¼d. ,,
Procaine hydrochloride
Pyridine 90/160 22s. 6d. g.
Quinine sulphate 1s. 9½d. oz.
Riboflavine 5½d. g.
Saccharine
Soluble 80s. 10d. lb.
Insoluble 99s. 10d. ,,
Salicylic acid 3s. 2½d. ,,
Silver nitrate 5s. 2¾d. oz.
Sodium benzoate 2s. 7½d. lb. (ton)
Sodium carboxy methyl cellulose Tech. £185 ton
Sodium lauryl sulphate B.P. 4s. 6½d. lb.
Sodium salicylate 3s. 9d. lb. (ton)
Sorbitol
Powder 3s. 3d. lb.
Syrup 1s. 9½ ,,
Stannic chloride 8s. 11d. ,,
Stannous chloride 9s. 5d. ,,
Strychine
Sulphaguanidine 11s. lb. (cwt.)
Sulphanilamide 5s. 9d. ,, ,,
Sulphathiazol 15s. ,, ,,
Tannic acid B.P. Levis 10s. ,, ,,
Tartaric acid B.P. 292s. cwt. (ton)
Terpineol B.P. 2s. 4½d. lb.
Theophylline B.P. 31s. 6d. kg.
Thiamine hydrochloride 25s. per 100 g.
Thiourea 5s. 7d. per ,,
***a*-Tocopherol** 23s. per 25 g.
Trichloroacetic acid 10s. lb.
Triethanolamine £206 ton
Urea B.P. 9d. lb.
Vanillin 25s. 6d.-30s. lb.
Zinc oxide B.P. £101 (ton)

INDUSTRIAL SOLVENTS

Acetone £84 ton
Amyl acetate B.S.S. £251 ,,
Amyl alcohol B.S.S. £256 ,,
Benzene B.P.C. 1s. 8d. lb.
***n*-Butyl acetate** £169 ton
***n*-Butyl alcohol** £137 10s. ,,
Ether (diethyl ether) B.S.S. 2s. lb.
Ethyl acetate £137 ton
Ethyl alcohol Synthetic 95% B.P. 3s. 5d. gal. (100 gal.)
Methylated spirits (Industrial)
Perfumery 44 o.p. 6s. 11d. gal.
74 o.p. 7s. 6d. gal.
Methyl ethyl ketone £134 10s. ton
Methyl isobutyl carbinol £159 ,,
Methyl isobutyl ketone £165 ,,
Diethyl phthalate £204 ,,
Dimethyl phthalate £197 ,,

OILS AND FATS

Palm kernel oil £108 ton ex works
Palm oil £102 ,, ,,
Stearine, T.P. Flake £148 ton

GUMS AND WAXES

Agar Agar No. 1 16s. 6d. lb.
Beeswax, Dar-es-Salaam £21 5s. cwt. ex works
Benzoin £26 10s. cwt.
Candelilla £23 5s. ,,
Carnauba, Prime Yellow £35 10s. ,,
Gum arabic lump £9 ,,
Karaya powder 3s. 4d. lb.
Paraffin wax £77 ton
Peru balsam 10s. lb.
Shellac, No. 1 £10 17s. 6d. cwt.
Tragacanth, No. 1 152s. 10d. ,,

GENERAL CHEMICALS

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Di- £97 10s. ,,
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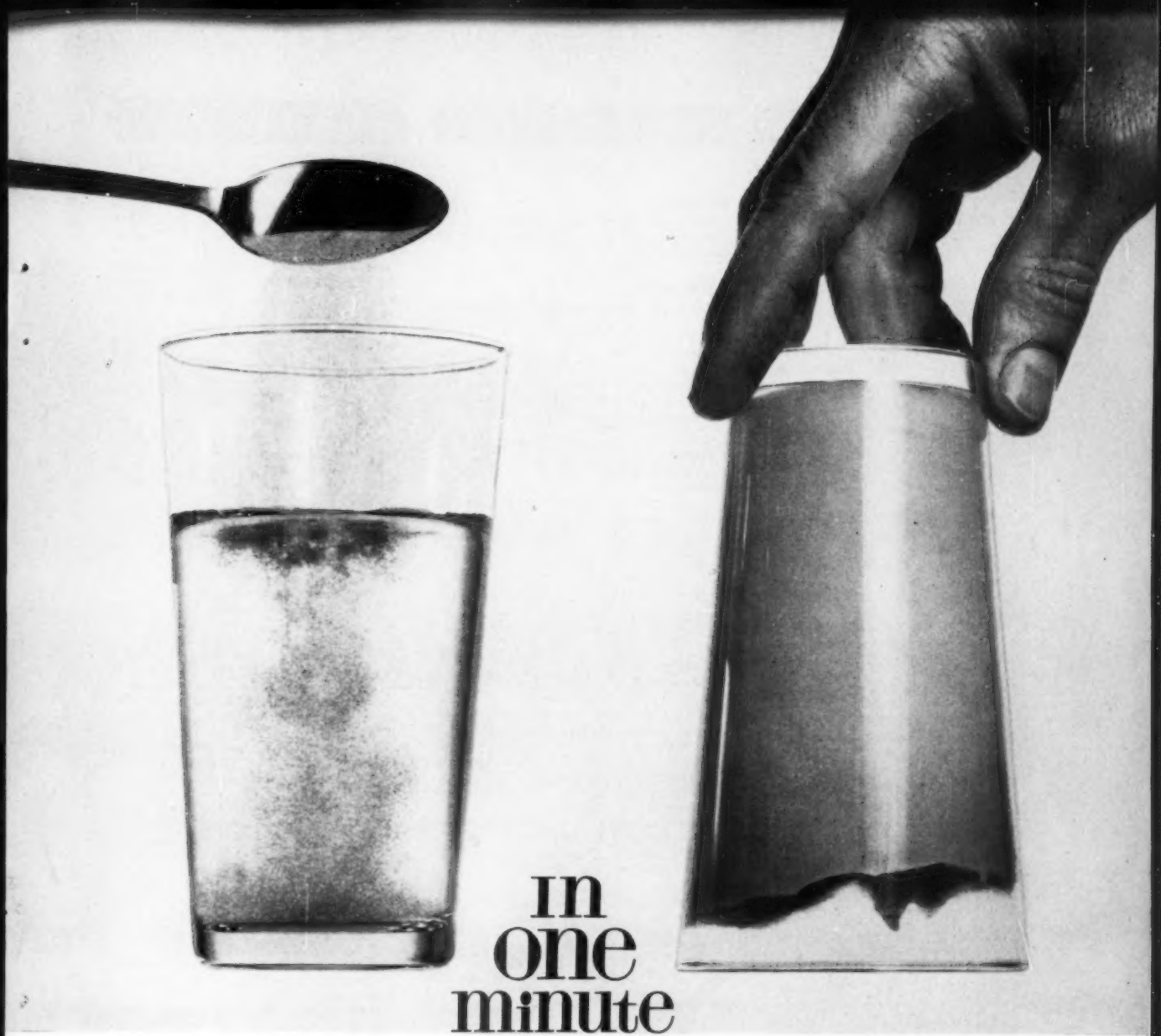
Sodium sulphide flake £40 12s. 6d. ,,
Sodium sulphite Tech. Crystal £27 5s. ,,
Sodium tripolyphosphate £95 ,,
Sulphuric acid Tech. £14 ton carboys
Zinch chloride Tech. 115s. cwt.



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ULSWELL.—812,977. *T.W. Reynolds Ltd.*

PROBIOVIT.—812,028. *Istituto Farmacoterapico Italiano S.A.*

TRI-ADCORTYL. — 812,104. *E. R. Squibb and Sons Ltd.*

SUXINUTIN.—812,275. *Parke, Davis and Co.*

ALDERCILLIN.—814,036. *I.C.I. Ltd.*

MYOGESIC.—818,357. *Chas Pfizer and Co. Inc.*

SLIMCAL.—814,005. *A. Wander Ltd.*

KOPLIVAX.—814,427. *The Wellcome Foundation Ltd.*

AMYLOZINE.—814,478. *Smith Kline and French Laboratories Ltd.*

TABPEN.—815,628. *The Distillers Co. (Biochemicals) Ltd.*

STENOROL.—815,884. *Les Laboratoires Français de Chimiotherapie S.A.*

CERNILTON.—815,793. *Aktiebolaget Cernelle.*

HYCOTAN.—816,563. *Duncan, Flockhart and Co. Ltd.*

KILDRUFF.—816,752; ENDRUFF.—816,753. *William Urquhart-Dykes.*

COLPHEN.—817,766. *Riker Laboratories Ltd.*

ARC.—806,192. *County Laboratories Ltd.*

UNICEL.—813,494; AVLOMYCIN.—813,897. *I.C.I. Ltd.*

TIGLYSSIN.—814,050. *Duncan, Flockhart and Co. Ltd.*

HUNTARIA.—814,249. *Armour and Co.*

SPARTASE.—815,911. *American Home Products Corp.*

TRYPTIZOL.—816,901; AMBITROP.—816,902. *Merck and Co. Inc.*

FARMINTIC.—818,239. *I.C.I. Ltd.*

HEXYMENTUS.—818,873. *Meggeson and Co. Ltd.*

DESTRAL.—819,263. *Borax Consolidated Ltd.*

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Dyestuffs of the tetra-azaporphin series and their production. *Badische Anilin- and Soda-Fabrik A.G.* 868,913.

Production of green trisazo dyestuffs. *Badische Anilin- and Soda-Fabrik A.G.* 870,698.

Heterocyclic monoazo dyestuffs and their chromium and cobalt complex compounds. *Westminster Bank Ltd.* 869,031.

Steroids

9 α-halosteroids. *G. D. Searle and Co.* 868,897.

Steroid compounds and process for their manufacture. *Ciba Ltd.* 868,975.

Heterocyclically substituted steroids. *Ciba Ltd.* 869,007.

6-methyl-3-oxo- Δ^4, ^{6}-steroid compounds. *British Drug Houses Ltd.* 870,286.

Steroid compounds and the preparation thereof. *Chas. Pfizer and Co. Inc.* 870,387, 870,388, 870,389, 870,390.

Antibiotics

Antibiotics. *Glaxo Laboratories Ltd.* 868,958.

Substances produced by penicillin-producing moulds. *Beecham Research Laboratories Ltd.* 870,396.

Antibiotic designated A7907 and processes for its manufacture. *Ciba Ltd.* 868,972.

Antibacterial agents. *Beecham Research Laboratories Ltd.* 876,516.

Antibacterial agents. *Beecham Research Laboratories Ltd.* 876,662.

Solubilisation of ostreogrycin antibiotics. *Glaxo Laboratories Ltd.* 875,702.

Substances having antibiotic activity. *Beecham Research Laboratories Ltd.* 876,508.

New patents are from the *Journal of Patents*, and new trade marks are from the *Trade Marks Journal*. In each case permission to publish has been given by the controller of Her Majesty's Stationery Office. Each of the publications mentioned is obtainable from the Patent Office, 26 Southampton Buildings, London, W.C.2.

NEW COMPANIES

These particulars of new companies have been extracted from the daily register of Jordan and Sons Ltd., company registration agents, Chancery Lane, London, W.C.2.

Dellson Pharmaceutical Co. Ltd. 22.8.61. 413 Hoe St., London, E.17. £100. Dirs.: E. G. Mastin and W. H. Watson.

S. P. R. Tullett (Salfords Pharmacy) Ltd. 22.8.61. 329 High Holborn, London, W.C.1. £3,500. Dirs.: Sylvia P. R. and Lenora E. Tullett.

Aster Packing Co. Ltd. 22.8.61. Swanfield Rd., Waltham Cross. £100. Packers of and dlrs. in cosmetics, pharmaceutical preparations, etc. Dirs.: Lauro Resta, Tadeusz Rumian, Laurino Ferrari and Domenico Ferrari.

G. J. Erlich Ltd. 23.8.61. £100. Mnfrs. importers and distributors of plastic and chemical materials, etc. Dirs.: George J. Erlich and Mrs. Dorota W. Erlich, 63 Dudley Court, Upper Berkeley St., London, W.1.

Produits de Beauté Juvena (G.B.) Ltd. 23.8.61. 229A Shaftesbury Avenue, London, W.C.2. £100. Mnfrs. of and dlrs. in cosmetic, chemical and medical substances, etc. Dirs.: Andrew Martin, George Winter and Ernest G. Locher.

R. Berkley (Chemists) Ltd. 24.8.61. 61 Beulah Rd., London, E.17. £1,000. Dirs.: Raymond and Doreen Berkley.

ITA Manufacturing Co. Ltd. 24.8.61. Swanfield Rd., Waltham Cross. £100. Mnfrs. of and dlrs. in industrial cosmetics and cosmetics of all kinds, etc. Dirs.: Lauro Resta, Laurino Ferrari and Domenico Ferrari.

Trafalgar Pharmaceutical Society Ltd. 25.7.61. Subs.: Anthony D. Smith and Bernard Hollingsworth, 2 South Sq., Grays Inn, W.C.1.

Riz of Bond Street Ltd. Mnfrs. of and dlrs. in chemicals, drugs, etc. Subs.: K. W. O'Neil and D. E. Franklyn (solr.), 158 Fenchurch St., E.C.3.

R. Pilkington (Chemist) Ltd. 20.7.61. 40 Upton Road, Claughton, Birkenhead. £5,000. Dirs.: Roy and Alice M. Pilkington.

Waun Pharmacy Ltd. 21.7.61. 30 Darwin Road, Port Talbot, Glam. To take over bus. of chemist cd. on at 21 Carmel Street, Gwaun-cae-Gurwen, by G. Williams. £400. Dirs.: G. Williams and Arthur L. Acraman.

Park House Pharmacy Ltd. 24.7.61. 406 Bank Chambers, 329 High Holborn, London, W.C.1. £6,000. Dirs.: Woolf and Thelma R. Kaicener.

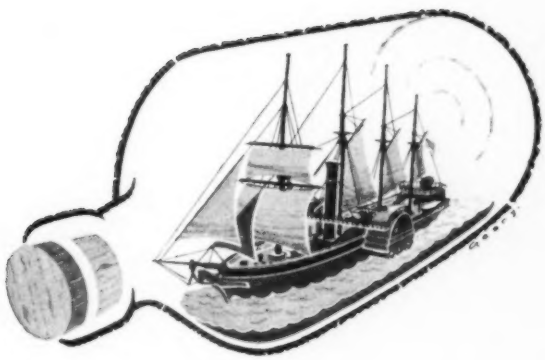
Sixty-Five Years Ago

From MANUFACTURING CHEMIST

October 1896

Kelvin supports kinetic theory

Lord Kelvin boldly denies the reputed failure of the atomic theory. "I am as much convinced as ever I was," remarks his lordship in a recent letter, "of the absolute truth of the Kinetic theory of gases. All I know is that I have not succeeded, in spite of 50 years' effort, in understanding more about the luminiferous ether, or the manner in which it operates in regard to the electrical and magnetic forces. It is upon this point that I remain as ignorant as I was 50 years ago, when I first became convinced that the ether operates essentially in all these actions."



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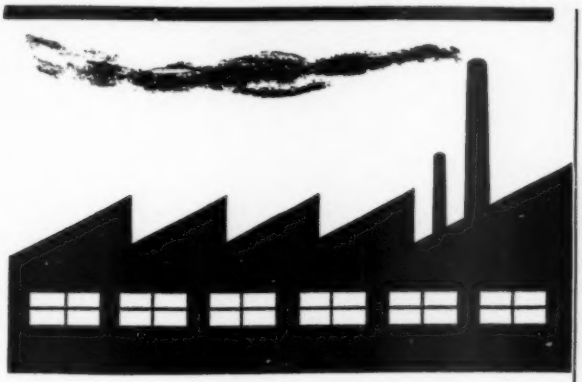

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TIB. 22

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(Mrs. Gaskell)

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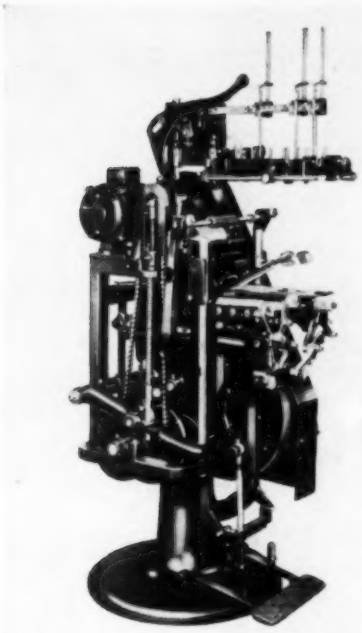

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MESSRS. L. B. BUTTERS & CO.
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As a result of continued expansion and the consequent emphasis placed on Development work we require one or at the most two chemists of proven ability.
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The Company manufactures a wide range of plastic sheeting and the Head Office and Works are situated in the North West within easy reach of pleasant residential surroundings. Experience in the plastics field would be useful but not essential; the main requirement is the ability to translate ideas into practical reality as quickly as possible.
Salary will be negotiated individually according to age and experience.
Conditions of employment include a contributory Superannuation Fund, Group Life Assurance Scheme, Sports and Social Club, Canteen facilities, etc.
Applications from interested candidates should be addressed to the Personnel Manager, Box 3080B, *Manufacturing Chemist*, 9, Eden Street, London, N.W.1.

PHARMACIST REQUIRED IN H.M. PRISON SERVICE

(Open to MEN and WOMEN registered Pharmacists)

MAN or WOMAN aged 25 or over required for position as Senior Pharmacist at H.M. Prison, Wormwood Scrubs, London, W.12. Salary scale £770-£1,010. Plus London Weighting of between £20-£50.

STARTING PAY ABOVE MINIMUM in some cases for previous N.H.S., Government Service or other comparable experience. ADDITIONAL ALLOWANCE of £25 for higher qualifications.

FIVE-DAY WEEK. POST SUPERANNUABLE under N.H.S. superannuation scheme. Annual leave allowance of 3 weeks and 3 days (4 weeks after 10 years service) plus 8½ days paid public and privilege holidays.

Apply Establishment Officer, Prison Commission, Horseferry House (JB530), Dean Ryle Street, London, S.W.1.

SALES MANAGER — PAKISTAN

MERCK SHARP & DOHME LTD,

seeks a SALES MANAGER aged 30 to 40, preferably married, with proven experience in sales management and administration within the ethical pharmaceutical field. Reporting directly to the British Managing Director of the Pakistani Company to be located in Karachi, the position will involve substantial travel and full scope of responsibility for developing and training a sales force and for promoting the sales of pharmaceutical specialities as well as some bulk medicinal chemicals under the M.S.D. label. Only British or Commonwealth subjects presently occupying sales managerial or equivalent positions at the assistant sales manager level or above are invited to apply. Candidates with previous experience in Pakistan or in India are preferred although such experience is not a definite requirement. Salary open and commensurate with experience and qualifications.
Candidates should send full particulars with photograph and date of availability to the Managing Director, Merck Sharp & Dohme Limited, Hoddesdon, Herts.

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required, with experience of pilot scale fine chemical drug manufacture. The post offers an excellent opportunity for experienced well qualified organic chemist, with good academic backround. Write in first instance giving full particulars to: The Managing Director, Biorex Laboratories Ltd., 47/51, Exmouth Street, London, E.C.1.

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SITUATIONS VACANT

. . . Continued on Page A96

SITUATIONS VACANT

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(Open to Men and Women registered Pharmacists)

MAN or WOMAN aged 25 or over required for a Category I Post at H.M. Prison, Durham. Salary scale £815-£1,110.

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FIVE-DAY WEEK. POST SUPERANNUABLE under N.H.S. superannuation scheme. Annual leave allowance of 3 weeks and 3 days (4 weeks after 10 years service) plus 8½ days paid public and privilege holidays.

Apply Establishment Officer, Prison Commission, Horseferry House (JB531), Dean Ryle Street, London, S.W.1.

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MERCK SHARP & DOHME LTD.

seeks a PRODUCTION MANAGER aged 30 to 40, preferably married, with proven practical experience in the manufacture of ethical pharmaceuticals plus some background in moderately complex medicinal chemical manufacturing on a semi-commercial scale, initially from intermediates. Reporting directly to the British Managing Director of the Pakistani Company to be located in Karachi, the position will involve complete responsibility for the activities of 20-25 people primarily engaged on the pharmaceutical side. Only British or Commonwealth subjects are invited to apply. Candidates with some experience of service in Pakistan or India would be preferred. Salary open and commensurate with experience and qualifications.
Candidates should send full particulars with photograph and date of availability to the Managing Director, Merck Sharp & Dohme Limited, Hoddesdon, Herts.

TRADE ANNOUNCEMENT

NICHOLAS Laboratories Ltd. It is announced that Nicholas Laboratories Ltd. have been appointed as Managing and Distributive agents for British Schering Ltd. in respect of all world markets. The sales forces of both British Schering and Nicholas Laboratories will retain their separate identities and will be headed by Mr. A. J. Whelan and Mr. T. Addey respectively. This change will be immediately effective and, as a consequence, orders and letters for British Schering Ltd. should, from now onward, be sent to 225, Bath Road, Slough, Bucks. Tel.: Slough 23971.

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Ref. B.660. British. Male. Married. Age 33. H.N.C. (Mech. Eng.), A.M.I.E.T. Dip. in Boiler inspectn. & maint. 5 yrs. Locomotive Apprentice, 2 yrs. Supervising Boiler Maker, railway. 4 yrs. Asst. to Planned Maint. Engr., chem. works. 2 yrs. Design D/man, superheater designers. At present Design Engr., superheater designers. Studying for A.M.I.Mech.E. Seeks post as **DESIGN OR MAINT. ENGR.** London (N.W. or W.) or Slough area. £1,150 p.a.

Ref. B.661. British. Male. Married. Age 33. A.M.I.E.D. 5 yrs. Apprentice, aircraft mnfrs. 1 yr. D/man, P.O. research. 1 yr. D/man, motor control (elect.). 3 yrs. Design D/man, process control equipt. 2 yrs. Design D/man & 1 yr. Asst. Chief D/man, nuclear instruments. At present Design Engr. (electro-mech.) & Project Engr., nuclear instruments. Seeks post as **DESIGN ENGR.** London, S. London, N. Kent. £1,500 p.a.

Ref. B.662. British. Male. Married. Age 48. A.Inst.Gas Engrs. 5 yrs. Apprentice, mnfrs. elect. instruments. 2 yrs. D/man, elect. & radio mnfrs. 2 yrs. Engr., electronic test gear. 2 yrs. Design Engr., aircraft mnfrs. 5 yrs. Tech. Officer, ministry. 2 yrs. Sales Mgr., electronic instruments. At present Mgr. & Director, electronic instruments, automation, process control gear mnfrs. Wide knwlge. prod. sales & mgt. a/cs. Author tech. book & many articles. Seeks **MANAGEMENT APPOINTMENT** or post as **SALES MGR. (TECH.).** Anywhere. £2,000/£2,200 p.a.

Ref. B.663. British. Male. Married. Age 26. O.N.C. Has taken A.M.I.H. & V.E. exams. 3½ yrs. Asst. Design Engr., htg. & vent. contractor. 3 yrs. Asst. & Senr. Design Engr., h. & v. consultant. At present Senr. Design D/man, h. & v. consltg. engrs. Seeks post as **SENR. DESIGN D/MAN.** London. £1,250 p.a.

Ref. B.664. British. Male. Married. Age 45. 6 yrs. Prod. Engr. (tooling, design, etc.), mech. engrs. 4 yrs. Asst. to Director & Genl. Mgr., pressure diecasters. 4 yrs. Senr. Prod. Engr., domestic appliances. 2 yrs. Prod. Superintendent, pressure diecasters & engrs. 4½ yrs. Mgr. i/c factory, lamp making & wire dwg. 8 mnths. Prod. Superintendnet, domestic appliances. At present Genl. Prod. Mgr., electro-mech. engrs. Consid. exper. most aspects mngt., std costing, works & prod. control, programming, prod. engg. for batch or flow processes, l/out, tooling, plant & equipt., estimating, W.S. Seeks post as **GENL. WORKS OR PROD. MANAGER.** Essex, E. Anglia, Home Counties or London area. £1,550 p.a. approx.

Ref. B.665. British. Male. Single. Age 21. O.N.C. (Mech. Eng.). At present taking H.N.C. (Mech. Eng.). 1 yr. Trainee D/man, light engrs. 1 yr. Trainee Plastics Mouldmaker, mould makers. 2 yrs. Lab. Tech. & at present Research Asst., educ. institution. Seeks post as **TECH. SALES REPRESENTATIVE WITH PLASTICS COMPANY.** London or within 12-mile radius Surbiton. £650 p.a. approx.

Ref. B.666. British. Female. Single. Age 22. G.C.E. "A" level Chem. 2½ yrs. Lab. Asst., food specialists. 1 yr. Lab. Asst., hospital. Seeks post as **LABORATORY ASST.** Pref. Central London. £520 p.a. approx.

Ref. B.667. British. Male. Married. Age 40. B.Sc. (Physics, Chem.), M.Sc. (Org. Chem.). 1 yr. Research Chemist, paint mnfr. 6 yrs. Research Chemist, paint mnfrs. At present Research Chemist in edible oils, mnfr. soaps, detergents, cooking fats. Exper. mostly alkyd resin research & organic pigment research, & pilot plant work on cooking & spray dried fats. Seeks **RESPONSIBLE POST IN DEVELOPMENT WORKS.** U.K. (not London). £1,600 p.a.

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